

10/046,681

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 12:32:47 ON 12 NOV 2004

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 10 NOV 2004 HIGHEST RN 778546-63-7

DICTIONARY FILE UPDATES: 10 NOV 2004 HIGHEST RN 778546-63-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

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Uploading C:\Program Files\Stnexp\Queries\197974a.str

L1 STRUCTURE UPLOADED

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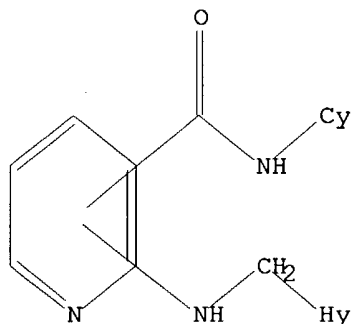
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L2 STRUCTURE UPLOADED

=> d 11

L1 HAS NO ANSWERS

L1 STR



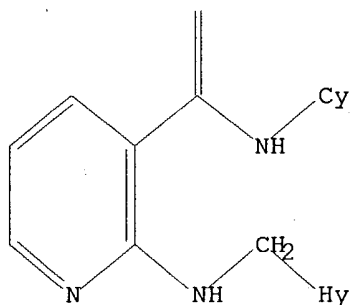
Structure attributes must be viewed using STN Express query preparation.

=> d 12

L2 HAS NO ANSWERS

L2 STR

10/046,681



Structure attributes must be viewed using STN Express query preparation.

=> s 11 sss full

FULL SEARCH INITIATED 12:35:10 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 699857 TO ITERATE

57.2% PROCESSED 400000 ITERATIONS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.11

542 ANSWERS

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **INCOMPLETE**
PROJECTED ITERATIONS: 699857 TO 699857
PROJECTED ANSWERS: 856 TO 1040

L3 542 SEA SSS FUL L1

=> s 12

SAMPLE SEARCH INITIATED 12:35:25 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 160 TO ITERATE

100.0% PROCESSED 160 ITERATIONS
SEARCH TIME: 00.00.01

28 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 2442 TO 3958
PROJECTED ANSWERS: 243 TO 877

L4 28 SEA SSS SAM L2

=> file caplus

COST IN U.S. DOLLARS

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |
| 157.10 | 157.31 |

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 12:35:57 ON 12 NOV 2004
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10/046,681

PRAI US 2001-261339P P 20010112
US 2001-323764P P 20010919
US 2002-46681 A2 20020110
US 2002-197974 A 20020717
OS MARPAT 140:16647

=> file caplus
COST IN U.S. DOLLARS

SINCE FILE TOTAL
ENTRY SESSION
2.38 159.69

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 12:37:49 ON 12 NOV 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 12 Nov 2004 VOL 141 ISS 20
FILE LAST UPDATED: 10 Nov 2004 (20041110/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 13
L8 11 L3

=> s 14
L9 3 L4

=> d 18 1-11 ibib abs hitstr

L8 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:515506 CAPLUS
DOCUMENT NUMBER: 141:71453
TITLE: Preparation of anthranilic acid amide derivatives as neoplastic inhibitors
INVENTOR(S): Bold, Guido; Furet, Pascal; Manley, Paul William
PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis Pharma GmbH
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2004052884 | A1 | 20040624 | WO 2003-EP14086 | 20031211 |

date not good

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 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

PRIORITY APPLN. INFO.:

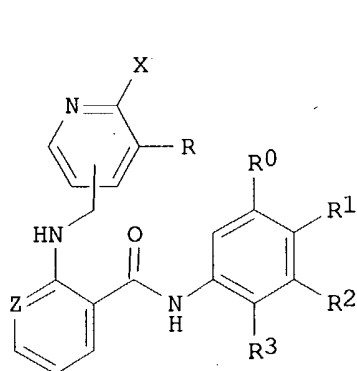
GB 2002-29022

A 20021212

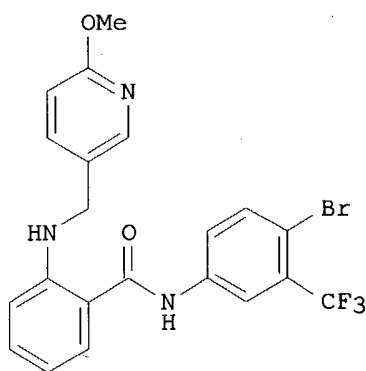
OTHER SOURCE(S):

MARPAT 141:71453

GI



I



II

AB The title compds. I [wherein R and R0 = independently H, halo, (un)substituted alkyl, alkenyl, alkynyl, aryl, heteroaryl, etc.; R1 = H, halo, (un)substituted alkyl, alkenyl, alkynyl, alkoxy, OCF3, OCH2CF3, OCH2CH2CF3, or OCH2CH2CH2CF3; R2 = perfluoroalkyl; R3 = H or halo; X = OH, alkoxy, alkylthio, imino, alkylimino, halo, etc.; Z = N or CH] or salts, N-oxides, or tautomers thereof are prepared as neoplastic inhibitors for the treatment of human or animal body. For example, the compound II was prepared in a multi-step synthesis. Formulations containing I as an active ingredient were also described.

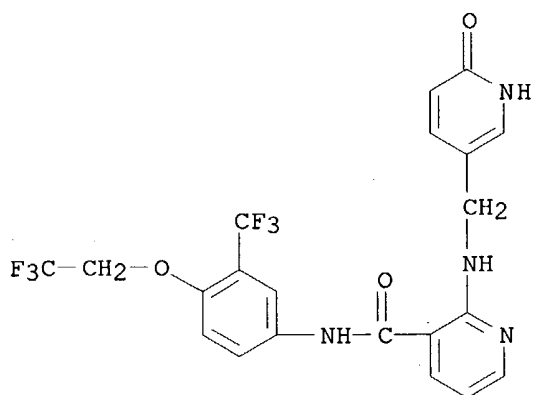
IT 709045-41-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of anthranilic acid amide derivs. as neoplastic inhibitors)

RN 709045-41-0 CAPLUS

CN 3-Pyridinecarboxamide, 2-[[[1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-(2,2,2-trifluoroethoxy)-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



L8 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:950057 CAPLUS

DOCUMENT NUMBER: 140:16647

TITLE: Preparation of 2-aminopyridine-3-carboxamides as remedies for angiogenesis mediated diseases

INVENTOR(S): Askew, Benny; Adams, Jeffrey; Booker, Shon; Chen, Guoqing; Dipietro, Lucian V.; Elbaum, Daniel; Germain, Julie; Geuns-Meyer, Stephanie D.; Habgood, Gregory J.; Handley, Michael; Huang, Qi; Kim, Tae-seong; Li, Aiwen; Nishimura, Nobuko; Nomak, Rana; Patel, Vinod F.; Riahi, Babak; Kim, Joseph L.; Xi, Ning; Yang, Kevin; Yuan, Chester Chenguang

PATENT ASSIGNEE(S): Amgen Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 252 pp., Cont.-in-part of U.S. Ser. No. 46,681.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

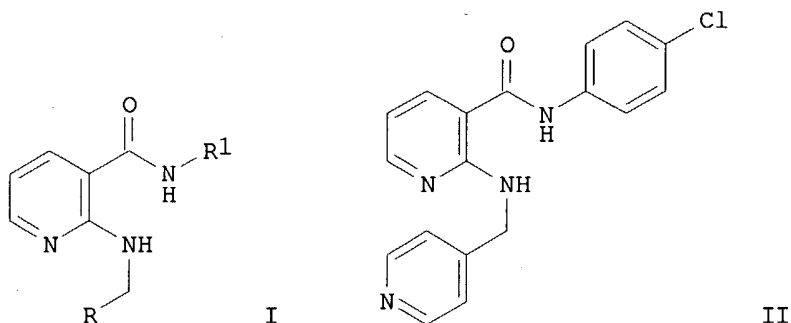
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 2003225106 | A1 | 20031204 | US 2002-197974 | 20020717 |
| US 2003125339 | A1 | 20030703 | US 2002-46681 | 20020110 |
| ZA 2003005197 | A | 20040319 | ZA 2003-5197 | 20030704 |
| WO 2004007458 | A1 | 20040122 | WO 2003-US22417 | 20030715 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: US 2001-261339P P 20010112
US 2001-323764P P 20010919
US 2002-46681 A2 20020110
US 2002-197974 A 20020717

OTHER SOURCE(S): MARPAT 140:16647

applies

GI



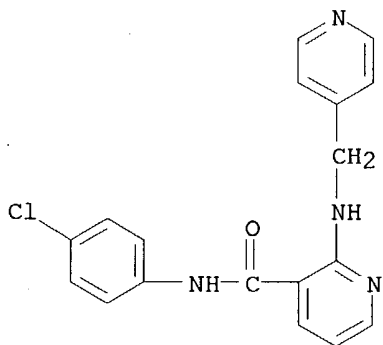
AB The title compds. [I; R = (un)substituted 4-pyridyl, 2-pyridyl, 4-pyrimidinyl, 4-quinolyl, etc.; R1 = (un)substituted aryl, cycloalkyl, 5-6 membered heteroaryl, 9-10 membered bicyclic and 11-14 membered tricyclic heterocyclyl], which are effective for prophylaxis and treatment of diseases and other maladies or conditions involving, cancer and the like, were prepared. Thus, the title compound II was prepared from 2-aminonicotinic acid, 4-chloroaniline, and 4-pyridinecarboxaldehyde. The compds. I showed inhibition of KDR kinase at $< 50 \mu\text{M}$. Many compds. I inhibited VEGF-stimulated HUVEC proliferation at a level below 50 nM. Pharmaceutical composition comprising the compound I is claimed.

IT 453561-03-0P 453561-73-4P 453561-77-8P
453561-95-0P 453562-69-1P 453562-83-9P
453563-07-0P 453563-37-6P 453563-79-6P
453564-01-7P 629651-31-6P 629651-56-5P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-aminopyridine-3-carboxamides for treating angiogenesis mediated diseases)

RN 453561-03-0 CAPLUS

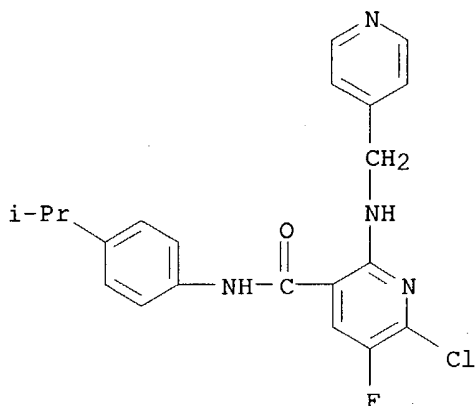
CN 3-Pyridinecarboxamide, N-(4-chlorophenyl)-2-[(4-pyridinylmethyl)amino]-
(9CI) (CA INDEX NAME)



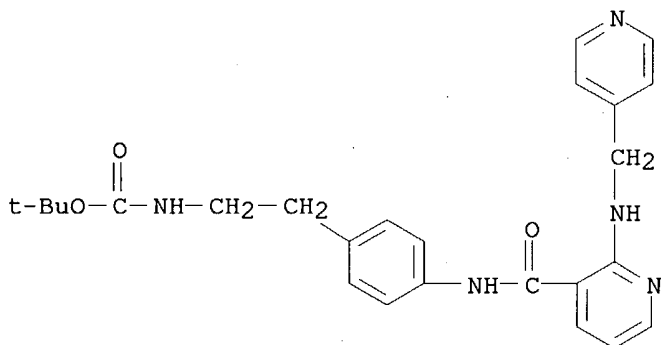
RN 453561-73-4 CAPLUS

CN 3-Pyridinecarboxamide, 6-chloro-5-fluoro-N-[4-(1-methylethyl)phenyl]-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

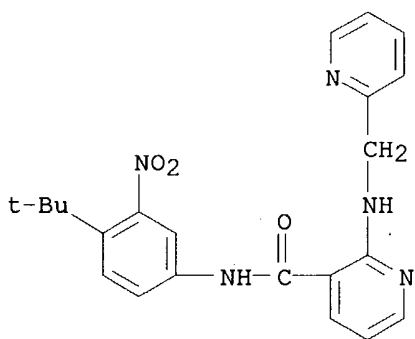
10/046,681



RN 453561-77-8 CAPLUS
CN Carbamic acid, [2-[4-[[[2-[(4-pyridinylmethyl)amino]-3-pyridinyl]carbonyl]amino]phenyl]ethyl]-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)



RN 453561-95-0 CAPLUS
CN 3-Pyridinecarboxamide, N-[4-(1,1-dimethylethyl)-3-nitrophenyl]-2-[(2-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

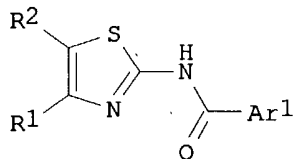


RN 453562-69-1 CAPLUS
CN 3-Pyridinecarboxamide, N-(2,3-dihydro-3,3-dimethyl-1H-indol-6-yl)-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

10/046,681

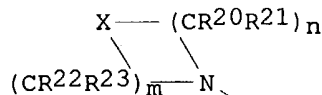
L8 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:591177 CAPLUS
DOCUMENT NUMBER: 139:149652
TITLE: Preparation of 2-acylaminothiazole derivatives or salts thereof as c-Mpl receptor ligands
INVENTOR(S): Sugasawa, Keizo; Watanuki, Susumu; Koga, Yuji; Nagata, Hiroshi; Obitsu, Kazuyoshi; Wakayama, Ryutaro; Hirayama, Fukushi; Suzuki, Ken-ichi
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2003062233 | A1 | 20030731 | WO 2003-JP270 | 20030115 |
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| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1466912 | A1 | 20041013 | EP 2003-700571 | 20030115 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| PRIORITY APPLN. INFO.: JP 2002-10413 A 20020118 JP 2002-10447 A 20020118 WO 2003-JP270 W 20030115 | | | | |
| OTHER SOURCE(S): MARPAT 139:149652 | | | | |
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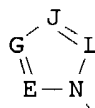


I

Q=



Q1=



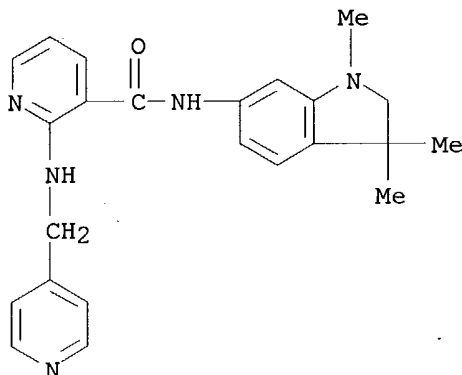
AB 2-Acylaminothiazole derivs. or pharmaceutically acceptable salts thereof [I; Ar1 = each (un)substituted aryl, monocyclic aromatic heterocyclyl, or bicyclic condensed heterocyclyl; R1 = each (un)substituted aryl or monocyclic aromatic heterocyclyl; R2 = Q, Q1, R24R25N; wherein n, m = an integer of 1-3; when n or m is an integer of ≥2, CR20R21 and CR22R23 may represent a different group; X = O, S, NR26, C(R27)R28; E, G, J, L = N, CR29; R20-R23, R26-R29 = H, OH, lower alkoxy, each (un)substituted lower alkyl, cycloalkyl, aryl, arylalkyl, aromatic heterocyclyl, aromatic heterocyclylalkyl, nonarom. heterocyclyl, lower

date not soq

10/046,681

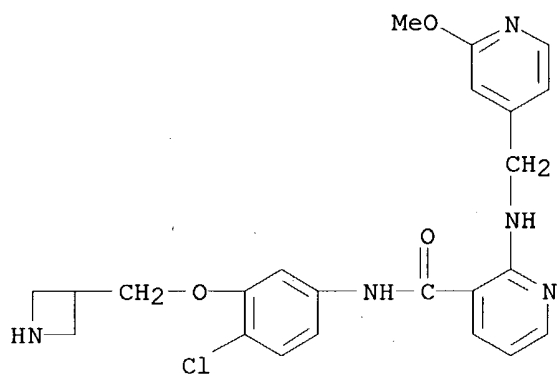
RN 629651-86-1 CAPLUS

CN 3-Pyridinecarboxamide, N-(2,3-dihydro-1,3,3-trimethyl-1H-indol-6-yl)-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)



RN 629651-87-2 CAPLUS

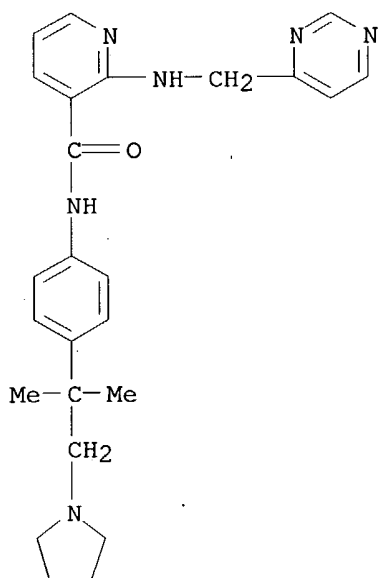
CN 3-Pyridinecarboxamide, N-[3-(3-azetidylmethoxy)-4-chlorophenyl]-2-[[2-methoxy-4-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)



RN 629651-88-3 CAPLUS

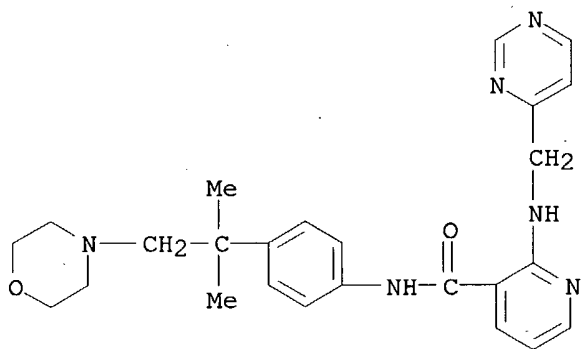
CN 3-Pyridinecarboxamide, N-[4-[1,1-dimethyl-2-(1-pyrrolidinyl)ethyl]phenyl]-2-[(4-pyrimidinylmethyl)amino]- (9CI) (CA INDEX NAME)

10/046,681



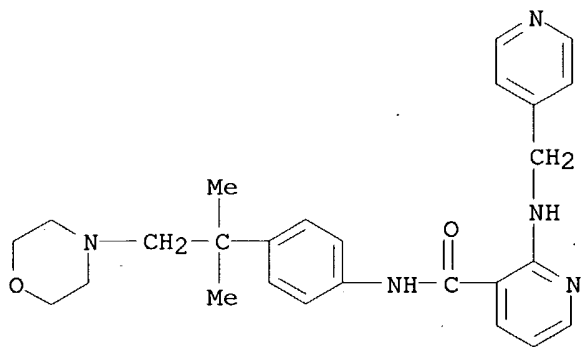
RN 629651-89-4 CAPLUS

CN 3-Pyridinecarboxamide, N-[4-[1,1-dimethyl-2-(4-morpholinyl)ethyl]phenyl]-2-[(4-pyrimidinylmethyl)amino]- (9CI) (CA INDEX NAME)



RN 629651-90-7 CAPLUS

CN 3-Pyridinecarboxamide, N-[4-[1,1-dimethyl-2-(4-morpholinyl)ethyl]phenyl]-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)



10/046,681

L8 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:551181 CAPLUS

DOCUMENT NUMBER: 139:117339

TITLE: Preparation of substituted arylamine derivatives as antitumor agents

INVENTOR(S): Elbaum, Daniel; Askew, Benny; Booker, Shon; Germain, Julie; Habgood, Gregory; Handley, Michael; Kim, Tae-Seong; Li, Aiwon; Nishimura, Nobuko; Patel, Vinod F.; Yuan, Chester Chenguang; Kim, Joseph L.

PATENT ASSIGNEE(S): Amgen Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 106 pp., Cont.-in-part of U.S. Ser. No. 46,526.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

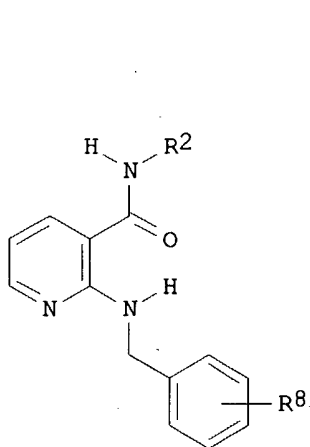
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

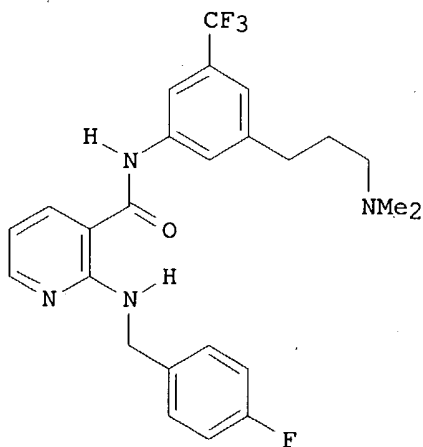
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| US 2003134836 | A1 | 20030717 | US 2002-197960 | 20020717 |
| US 2002147198 | A1 | 20021010 | US 2002-46526 | 20020110 |
| WO 2004007457 | A2 | 20040122 | WO 2003-US22276 | 20030715 |
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| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004204437 | A1 | 20041014 | US 2004-823809 | 20040412 |
| PRIORITY APPLN. INFO.: | | | US 2001-261360P | P 20010112 |
| | | | US 2001-323686P | P 20010919 |
| | | | US 2002-46526 | A2 20020110 |
| | | | US 2002-197960 | A 20020717 |

OTHER SOURCE(S): MARPAT 139:117339
GI

date not spec



I



II

AB The title compds. I [R2 = (un)substituted Ph, 9-10 membered bicyclic and 11-14 membered tricyclic (un)saturated heterocyclyl; R8 = halo, NH2, NO2, etc.], and their pharmaceutically acceptable derivs., are prepared and disclosed as agents effective for prophylaxis and treatment of diseases, such as angiogenesis mediated diseases. E.g., a multi-step synthesis of II, starting from 1-dimethylamino-2-propyne and 3-bromo-5-trifluoromethylaniline, was given. Selected compds. of the invention, e.g., II, inhibited VEGF-stimulated cell proliferation at a level below 50 nM. The invention encompasses novel compds., analogs, prodrugs and pharmaceutically acceptable derivs. thereof, pharmaceutical compns. and methods for prophylaxis and treatment of diseases and other maladies or conditions involving, cancer and the like.

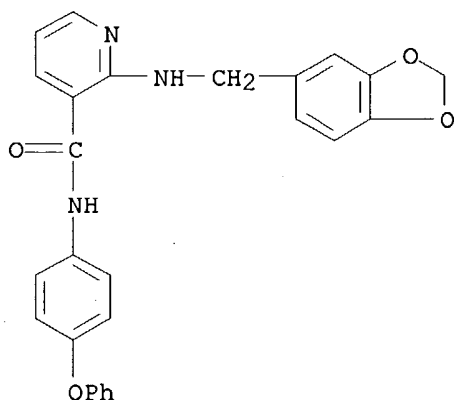
IT **442846-11-9P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(target compound; preparation of substituted aminopyridines as antitumor agents)

RN 442846-11-9 CAPLUS

CN 3-Pyridinecarboxamide, 2-[(1,3-benzodioxol-5-ylmethyl)amino]-N-(4-phenoxyphenyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:417626 CAPLUS

DOCUMENT NUMBER: 139:6865

TITLE: Nicotinoyl- or isonicotinoylaminobenzothiazoles as A2A receptor ligands

INVENTOR(S): Flohr, Alexander; Jakob-Roetne, Roland; Norcross, Roger David; Riemer, Claus

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 77 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2003043636 | A1 | 20030530 | WO 2002-EP12562 | 20021111 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, | | | | |

Date not good

10/046,681

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003134854 A1 20030717 US 2002-288100 20021105

US 6620811 B2 20030916

EP 1448198 A1 20040825 EP 2002-787632 20021111

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

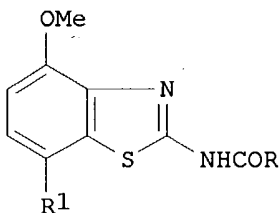
PRIORITY APPLN. INFO.:

EP 2001-127312 A 20011119

WO 2002-EP12562 W 20021111

OTHER SOURCE(S): MARPAT 139:6865

GI



AB Title compds. I [R = 2-substituted 4-pyridyl, 4-substituted 3-pyridyl; R1 = Ph, piperidin-1-yl, morpholinyl] were prepared for use as adenosine A2A receptor ligands. Thus, 4-methoxy-7-morpholinobenzothiazole-2-amine was acylated with 2-chloroisonicotinoyl chloride and treated with HOCH2CH2OMe to give I [R = 2-(2-methoxyethoxy)pyridin-4-yl, R1 = morpholino] which had a pKi for the human A2A receptor of 8.50.

IT 535923-69-4P 535923-96-7P

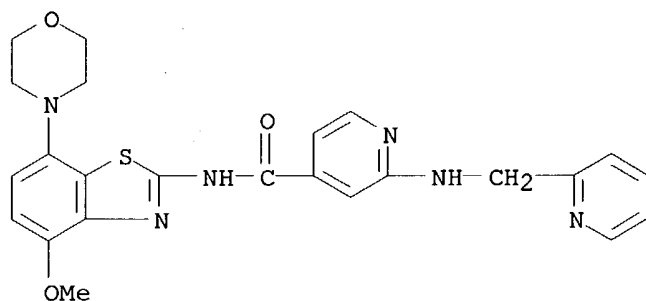
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nicotinoyl- or isonicotinoylaminobenzothiazoles as A2A receptor ligands)

RN 535923-69-4 CAPLUS

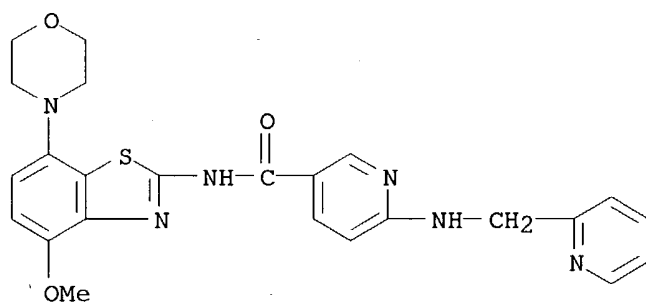
CN 4-Pyridinecarboxamide, N-[4-methoxy-7-(4-morpholinyl)-2-benzothiazolyl]-2-[(2-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

10/046,681



RN 535923-96-7 CAPLUS

CN 3-Pyridinecarboxamide, N-[4-methoxy-7-(4-morpholinyl)-2-benzothiazolyl]-6-[(2-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:868928 CAPLUS

DOCUMENT NUMBER: 137:352900

TITLE: Selective anthranilamide pyridine amides as inhibitors of VEGFR-2 and VEGFR-3

INVENTOR(S): Ernst, Alexander; Huth, Andreas; Krueger, Martin; Thierauch, Karl-Heinz; Menrad, Andreas; Haberey, Martin

PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany

SOURCE: PCT Int. Appl., 115 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

data not good

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2002090352 | A2 | 20021114 | WO 2002-EP4924 | 20020503 |
| WO 2002090352 | A3 | 20030501 | | |

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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|-------------|----|----------|------------------|----------|
| DE 10123574 | A1 | 20021128 | DE 2001-10123574 | 20010508 |
| DE 10125294 | A1 | 20021121 | DE 2001-10125294 | 20010515 |
| DE 10164590 | A1 | 20030710 | DE 2001-10164590 | 20011221 |
| EP 1392680 | A2 | 20040303 | EP 2002-735333 | 20020503 |

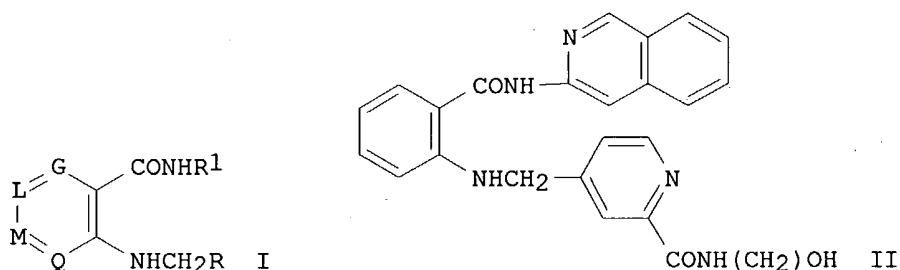
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

| | | | | |
|---------------|----|----------|----------------|----------|
| BR 2002009485 | A | 20040706 | BR 2002-9485 | 20020503 |
| JP 2004528379 | T2 | 20040916 | JP 2002-587431 | 20020503 |

PRIORITY APPLN. INFO.:

| | | |
|------------------|---|----------|
| DE 2001-10123574 | A | 20010508 |
| DE 2001-10125294 | A | 20010515 |
| DE 2001-10164590 | A | 20011221 |
| WO 2002-EP4924 | W | 20020503 |

OTHER SOURCE(S): MARPAT 137:352900
GI



AB Title compds. I [G, L, M, Q = N, (un)substituted CH, ≤ 1 of them being N; R = (un)substituted N heterocycle; R¹ = (un)substituted alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl] were prepared I are inhibitors of VEGFR-2 and VEGFR-3 and are used as medicaments for treating diseases that are caused by persistent angiogenesis, such as psoriasis, Kaposi's sarcoma, restenosis, such as e.g. stent-induced restenosis, endometriosis, Crohn's disease, Hodgkin's disease, leukemia, arthritis, such as rheumatoid arthritis, hemangioma, angiofibromatosis, in eye diseases such as diabetic retinopathy, neovascular glaucoma, in kidney diseases such as glomerulonephritis, diabetic nephropathy, malign nephrosclerosis, thrombic micro-angiopathic syndrome, transplant rejection and glomerulopathy, in fibrotic diseases such as hepatic cirrhosis, mesangial-cell proliferative diseases, arteriosclerosis, damage to the nerve tissue and inhibition of the re-occlusion of vessels after balloon catheter treatment, in vessel prosthetics or after the use of mech. devices for keeping vessels open, e.g. stents, as immunosuppressants, to support wound healing without scars and in cases of age spots and contact dermatitis. I can also be used as inhibitors of VEGFR-3 in lymphangiogenesis for hyperplastic and dysplastic changes in the lymphatic system. Thus, 2-amino-N-isoquinolin-3-ylbenzamide was treated with 2-bromo-5-pyridinecarboxaldehyde, followed by carboxylation and amidation to give the amide II. II had IC₅₀ for inhibition of VEGFR-2 of 40 nM and for inhibition of cytochrome 450 isoenzyme 2C9 of 2.9 μ M.

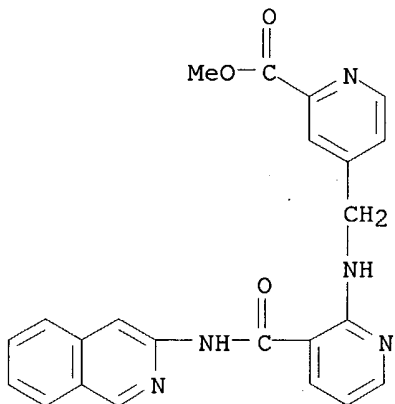
IT **474799-59-2**

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of isoquinolinylcarbamoylphenylaminomethylpyridinecarboxamides as VEGFR-2 and VEGFR-3 inhibitors)

10/046,681

RN 474799-59-2 CAPLUS

CN 2-Pyridinecarboxylic acid, 4-[[[3-[(3-isoquinolinylamino)carbonyl]-2-pyridinyl]amino]methyl]-, methyl ester (9CI) (CA INDEX NAME)



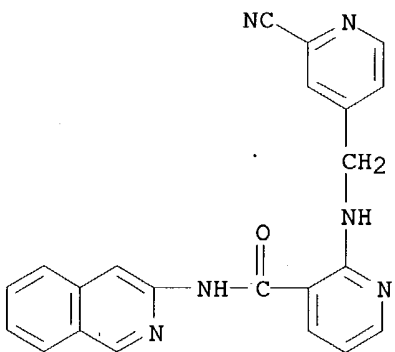
IT 474799-51-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of isoquinolinylcarbamoylethylphenylaminomethylpyridinecarboxamides as VEGFR-2 and VEGFR-3 inhibitors)

RN 474799-51-4 CAPLUS

CN 3-Pyridinecarboxamide, 2-[[[(2-cyano-4-pyridinyl)methyl]amino]-N-3-isoquinolinyl]- (9CI) (CA INDEX NAME)



IT 474799-25-2P 474799-26-3P

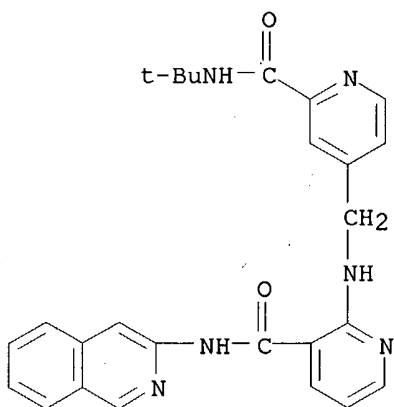
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of isoquinolinylcarbamoylethylphenylaminomethylpyridinecarboxamides as VEGFR-2 and VEGFR-3 inhibitors)

RN 474799-25-2 CAPLUS

CN 2-Pyridinecarboxamide, N-(1,1-dimethylethyl)-4-[[[3-[(3-isoquinolinylamino)carbonyl]-2-pyridinyl]amino]methyl]- (9CI) (CA INDEX NAME)

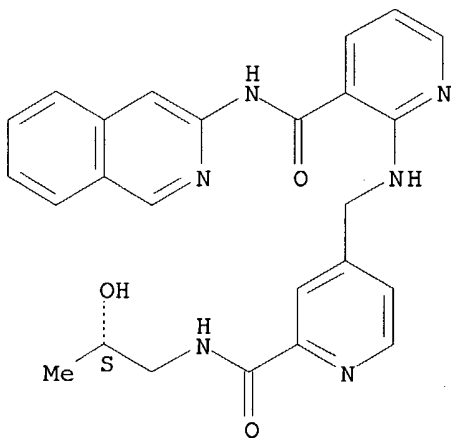
10/046,681



RN 474799-26-3 CAPLUS

CN 2-Pyridinecarboxamide, N-[(2S)-2-hydroxypropyl]-4-[[[3-[(3-isoquinolinylamino)carbonyl]-2-pyridinyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:868925 CAPLUS

DOCUMENT NUMBER: 137:352899

TITLE: Pyridylmethylantranilamide N-oxides as inhibitors of VEGFR II kinase

INVENTOR(S): Ernst, Alexander; Huth, Andreas; Krueger, Martin; Thierauch, Karl-Heinz; Menrad, Andreas; Haberey, Martin

PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany

SOURCE: PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

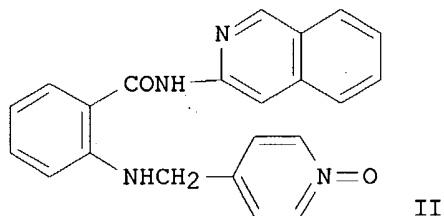
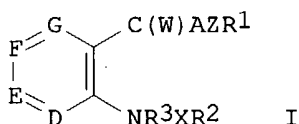
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|-------|-------|-----------------|-------|
| ----- | ----- | ----- | ----- | ----- |

data not good

WO 2002090349 A1 20021114 WO 2002-EP4923 20020503
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
DE 10123573 A1 20021128 DE 2001-10123573 20010508
DE 10125293 A1 20021121 DE 2001-10125293 20010515
EP 1389201 A1 20040218 EP 2002-740563 20020503
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2004528378 T2 20040916 JP 2002-587429 20020503
PRIORITY APPLN. INFO.: DE 2001-10123573 A 20010508
DE 2001-10125293 A 20010515
WO 2002-EP4923 W 20020503
OTHER SOURCE(S): MARPAT 137:352899
GI



AB Title compds. I [D, E, F, G = N, (un)substituted CH; A = (un)substituted NH; W = O, S, H2, (un)substituted NH; X, Z = (un)substituted alkylene; R1 = (un)substituted alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl; R2 = (un)substituted hetaryl N-oxide; R3 = H, alkyl] were prepared. These compds. can be used in the treatment of psoriasis, Kaposi's sarcoma, restenosis, endometriosis, Crohn's disease, Hodgkin's disease, leukemia, arthritis, such as rheumatoid arthritis, hemangioma, angiofibroma, eye diseases, such as diabetic retinopathy, neovascular glaucoma, renal diseases, such as glomerulonephritis, diabetic nephropathy, malignant nephrosclerosis, thrombotic microangiopathic syndromes, transplant rejections and glomerulopathy, fibrotic diseases such as cirrhosis of the liver, mesangial cell-proliferative diseases, arteriosclerosis, injuries of the nerve tissue, and for inhibiting the reocclusion of vessels after balloon catheter treatment, for use in vascular prosthetics or after inserting mech. devices for holding vessels open such as, e.g. stents, as immunosuppressants, as an aid in scar-free wound healing, and for treating age spots and contact dermatitis. They can also be used as VEGFR-3 inhibitors in lymphangiogenesis. Thus, the N-oxide II was obtained by reductive alkylation of 2-amino-N-isoquinolin-3-ylbenzamide with isonicotinaldehyde N-oxide and had IC50 for inhibition of VEGFR II of 0.03 μ M.

IT 352227-85-1P 474760-13-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

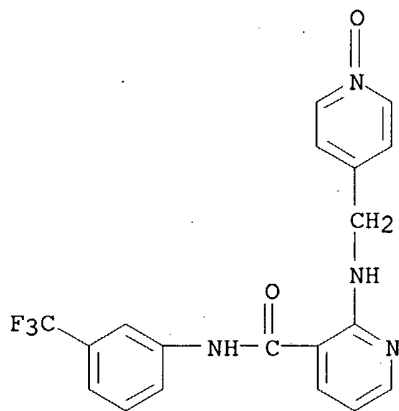
(preparation of pyridylmethylantranilamide N-oxides as inhibitors of VEGFR

10/046,681

II kinase)

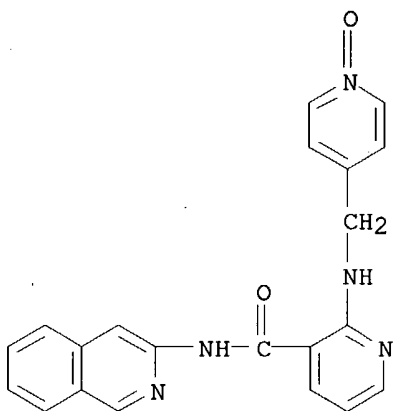
RN 352227-85-1 CAPLUS

CN 3-Pyridinecarboxamide, 2-[[[(1-oxido-4-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 474760-13-9 CAPLUS

CN 3-Pyridinecarboxamide, N-3-isoquinolinyl-2-[[[(1-oxido-4-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:658116 CAPLUS

DOCUMENT NUMBER: 137:201332

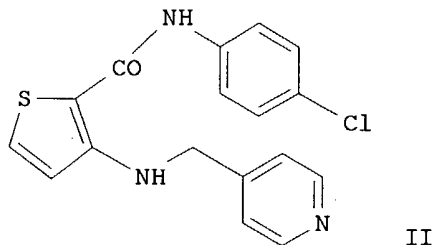
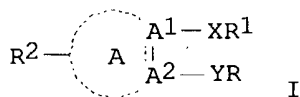
TITLE: Preparation of heterocyclalkylamine derivatives as remedies for angiogenesis mediated diseases

INVENTOR(S): Chen, Guoqing; Adams, Jeffrey; Bemis, Jean; Booker, Shon; Cai, Guolin; Croghan, Michael; Dipietro, Lucian; Dominguez, Celia; Elbaum, Daniel; Germain, Julie; Geuns-meyer, Stephanie; Handley, Michael; Huang, Qi; Kim, Joseph L.; Kim, Tae-seong; Kiselyov, Alexander; Ouyang, Xiaohu; Patel, Vinod F.; Smith, Leon M.; Stec, Markian; Tasker, Andrew; Xi, Ning; Xu, Shimin; Yuan,

applied

PATENT ASSIGNEE(S): Chester Chenguang
 SOURCE: Amgen Inc., USA
 PCT Int. Appl., 502 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2002066470 | A1 | 20020829 | WO 2002-US743 | 20020111 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| US 2003125339 | A1 | 20030703 | US 2002-46681 | 20020110 |
| BR 2002006435 | A | 20030923 | BR 2002-6435 | 20020111 |
| EP 1358184 | A1 | 20031105 | EP 2002-717325 | 20020111 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| EE 200300324 | A | 20031215 | EE 2003-324 | 20020111 |
| JP 2004531484 | T2 | 20041014 | JP 2002-565984 | 20020111 |
| ZA 2003005197 | A | 20040319 | ZA 2003-5197 | 20030704 |
| NO 2003003181 | A | 20030911 | NO 2003-3181 | 20030711 |
| PRIORITY APPLN. INFO.: | | | US 2001-261339P | P 20010112 |
| | | | US 2001-323764P | P 20010919 |
| | | | US 2002-46681 | A 20020110 |
| | | | WO 2002-US743 | W 20020111 |
| OTHER SOURCE(S): | MARPAT 137:201332 | | | |
| GI | | | | |



partially saturated heterocyclyl, 5-, or 6-membered heterocyclyl, 9-, or 10-membered fused partially saturated heterocyclyl, 9-, 10-, or 11-membered fused heteroaryl, naphthyl, 4-, 5-, or 6-membered cycloalkenyl; X = C:ZNR3, C:ZN(R3)R4; Z = O, S; Y = N:CH, NR5(CR6R7), R8N(R5)(CR6R7), NR5(CR6R7)R8; R = 5-, or 6-membered (un)substituted heterocyclyl, 9-, 10-, 11-membered heterocyclyl; R1 = 6-10-membered (un)substituted aryl, 5-, or 6-membered (un)substituted heterocyclyl, 9-11 membered (un)substituted fused heterocyclyl, cycloalkyl, cycloalkenyl; R2 = H, halo, oxo, SH, COOH, CHO; R3 = H, alkyl, 5-, or 6-membered heterocyclyl; R4 = alkylenyl, alkenylenyl, alkynylenyl; R5 = H, alkyl, aralkyl, C6H5; R6, R7 independently = H, halo, CN, alkyl; R6R7 = cycloalkyl; R8 = alkylenyl; etc.] are prepared and are effective for prophylaxis and treatment of diseases, such as angiogenesis mediated diseases. The invention encompasses novel compds., analogs, prodrugs and pharmaceutically acceptable derivs. thereof, pharmaceutical compns. and methods for prophylaxis and treatment of diseases and other maladies or conditions involving, cancer and the like. The subject invention also relates to processes for making such compds. as well as to intermediates useful in such processes. Thus, the title compound II was prepared from Me 3-amino-2-thiophenecarboxylate, 4-chloroaniline, and 4-pyridine carboxaldehyde via coupling reaction.

IT 453561-03-0P 453561-73-4P 453561-77-8P

453561-95-0P 453562-83-9P 453563-07-0P

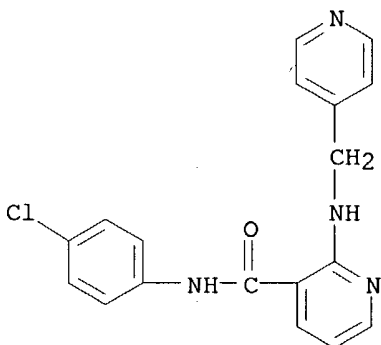
453563-37-6P 453563-79-6P 453564-01-7P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of heterocyclylalkylamine derivs. as remedies for angiogenesis mediated diseases)

RN 453561-03-0 CAPLUS

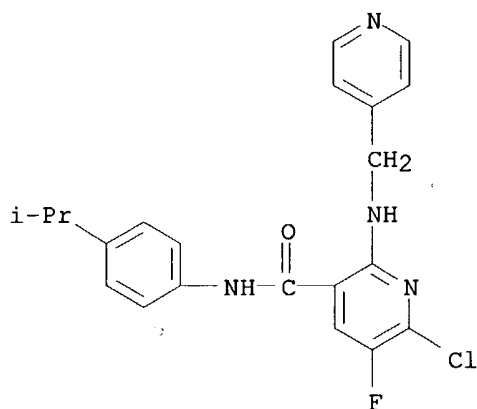
CN 3-Pyridinecarboxamide, N-(4-chlorophenyl)-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)



RN 453561-73-4 CAPLUS

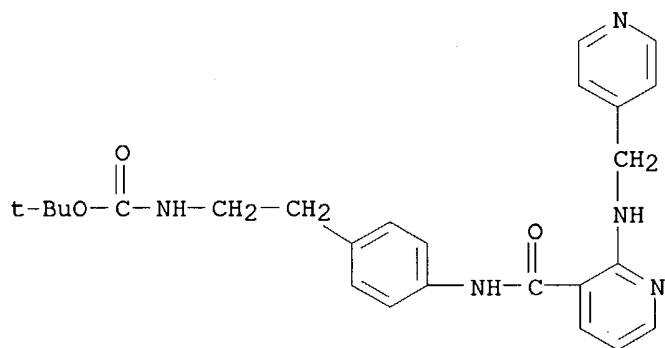
CN 3-Pyridinecarboxamide, 6-chloro-5-fluoro-N-[4-(1-methylethyl)phenyl]-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

10/046,681



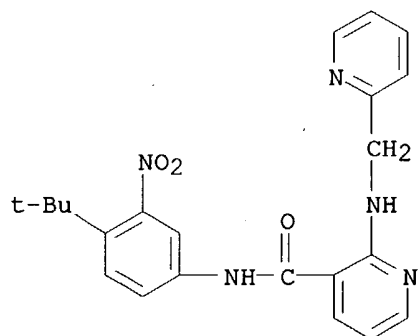
RN 453561-77-8 CAPLUS

CN Carbamic acid, [2-[4-[[[2-[(4-pyridinylmethyl)amino]-3-pyridinyl]carbonyl]amino]phenyl]ethyl]-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)



RN 453561-95-0 CAPLUS

CN 3-Pyridinecarboxamide, N-[4-(1,1-dimethylethyl)-3-nitrophenyl]-2-[(2-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

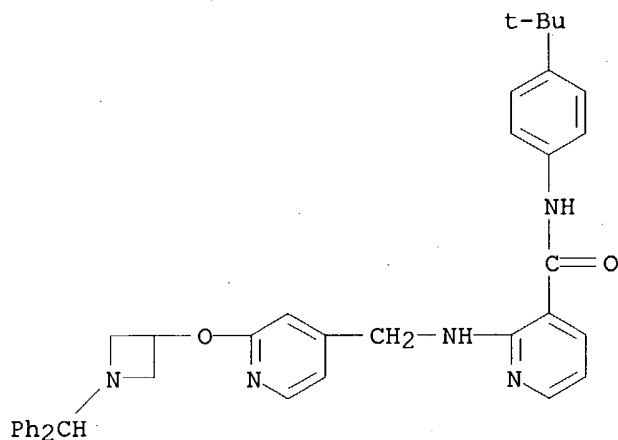


RN 453562-83-9 CAPLUS

CN 3-Pyridinecarboxamide, 2-[[[(2-chloro-4-pyridinyl)methyl]amino]-N-[4-(1,1-dimethylethyl)phenyl]- (9CI) (CA INDEX NAME)

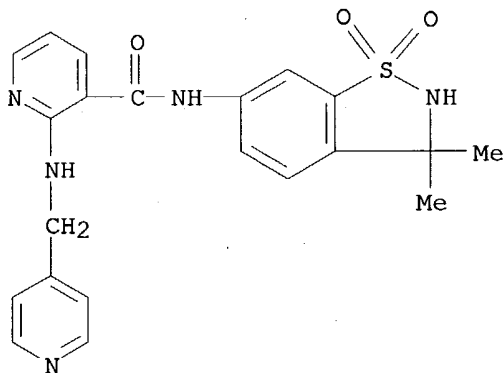
10/046,681

CN 3-Pyridinecarboxamide, N-[4-(1,1-dimethylethyl)phenyl]-2-[[[2-[[1-(diphenylmethyl)-3-azetidinyloxy]-4-pyridinyl]methyl]amino]- (9CI) (CA INDEX NAME)



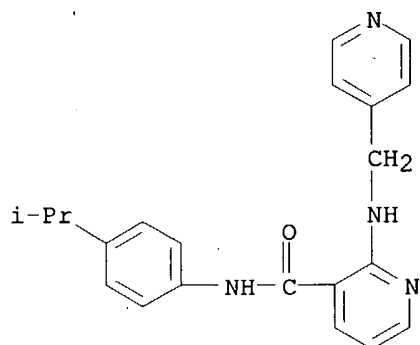
RN 453564-01-7 CAPLUS

CN 3-Pyridinecarboxamide, N-(2,3-dihydro-3,3-dimethyl-1,1-dioxido-1,2-benzisothiazol-6-yl)-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)



IT 352227-57-7P, 2-[(Pyridin-4-ylmethyl)amino]-N-(3-trifluoromethylphenyl)nicotinamide 352227-65-7P
352227-72-6P 352227-74-8P 453561-04-1P
453561-05-2P 453561-06-3P 453561-07-4P
453561-08-5P 453561-09-6P 453561-11-0P
453561-12-1P 453561-14-3P 453561-15-4P
453561-16-5P 453561-17-6P 453561-20-1P
453561-21-2P 453561-22-3P 453561-23-4P
453561-26-7P 453561-27-8P 453561-29-0P
453561-32-5P 453561-33-6P 453561-34-7P
453561-35-8P 453561-36-9P 453561-37-0P
453561-38-1P 453561-71-2P 453561-72-3P
453561-75-6P 453561-76-7P 453561-78-9P
453561-80-3P 453561-81-4P, 2-[(2,3-Dihydrobenzofuran-5-ylmethyl)amino]-N-[3,3-dimethyl-1-(piperidin-4-ylmethyl)-2,3-dihydro-1H-indol-6-yl]nicotinamide 453561-82-5P 453561-83-6P
453561-84-7P 453561-85-8P, N-[1-(2-Aminoacetyl)-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl]-2-[(2-methoxypyridin-4-

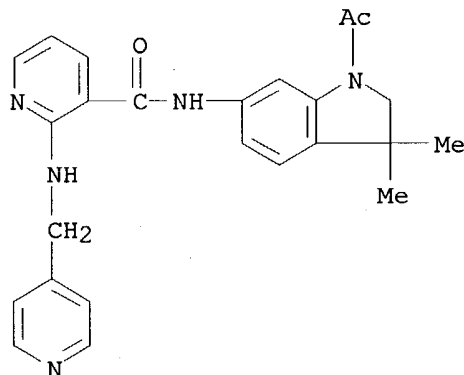
10/046,681



● x HCl

RN 453562-74-8 CAPLUS

CN 3-Pyridinecarboxamide, N-(1-acetyl-2,3-dihydro-3,3-dimethyl-1H-indol-6-yl)-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:539663 CAPLUS

DOCUMENT NUMBER: 137:109210

TITLE: Preparation of substituted arylamine derivatives and methods of use as antitumor agents

INVENTOR(S): Chen, Guoqing; Booker, Shon; Cai, Guolin; Croghan, Michael; Dipietro, Lucian; Dominguez, Celia; Elbaum, Daniel; Germain, Julie; Huang, Qi; Kim, Joseph L.; Kim, Tae-Seong; Patel, Vinod F.; Smith, Leon M.; Tasker, Andrew; Xi, Ning; Xu, Shimin; Yuan, Chester Chenguang

PATENT ASSIGNEE(S): Amgen Inc., USA

SOURCE: PCT Int. Appl., 253 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

*data
not good*

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2002055501 | A2 | 20020718 | WO 2002-US742 | 20020111 |
| WO 2002055501 | A3 | 20021219 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG US 2002147198 A1 20021010 US 2002-46526 20020110 EP 1358161 A2 20031105 EP 2002-717324 20020111 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR JP 2004531473 T2 20041014 JP 2002-556173 20020111 PRIORITY APPLN. INFO.: US 2001-261360P P 20010112 US 2001-323686P P 20010919 US 2002-46526 A 20020110 WO 2002-US742 W 20020111 OTHER SOURCE(S): MARPAT 137:109210 GI | | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [B1 and B2 independently equal C or N, wherein B1B2 form part of 5-6 membered heteroaryl ring A; R1 = one or more substituents selected from H, halo, oxo, (un)substituted cycloalkyl, phenylalkyl, etc.; R2 = (un)substituted cycloalkyl, cycloalkenyl, 6-10 membered aryl or 5-6 membered heterocyclyl, etc.; R3 = (un)substituted aryl; R4 = H, alkyl, (un)substituted Ph or aralkyl; X1 = bond, alkylene, alkenylene and alkynylene, where one of the CH2 groups may be substituted with O or NH, wherein X1 is optionally substituted with OH; X2 = (un)substituted N containing linker, e.g., -NHCH2-, and there pharmaceutically acceptable derivs., are prepared and disclosed as agents effective for prophylaxis and treatment of diseases, such as angiogenesis mediated diseases. Thus, II was prepared via arylation of 1-dimethylamino-2-propyne with 3-bromo-5-trifluoromethylaniline, hydrogenation, amidation with 2-chloropyridine-3-carbonyl chloride and chloro-substitution with 4-fluorobenzylamine. Selected compds. of the invention, e.g., II, inhibited VEGF-stimulated cell proliferation at a level below 50 nM. The invention encompasses novel compds., analogs, prodrugs and pharmaceutically acceptable derivs. thereof, pharmaceutical compns. and methods for prophylaxis and treatment of diseases and other maladies or conditions involving, cancer and the like.

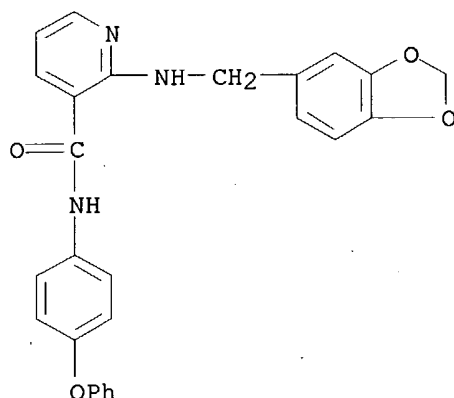
IT 442846-11-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(target compound; preparation of substituted aminopyridines as antitumor agents)

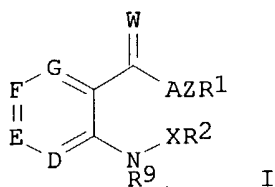
RN 442846-11-9 CAPLUS

CN 3-Pyridinecarboxamide, 2-[(1,3-benzodioxol-5-ylmethyl)amino]-N-(4-phenoxyphenyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2001:833303 CAPLUS
 DOCUMENT NUMBER: 135:357941
 TITLE: Preparation of aminoheteroarylcarboxamides as vascular endothelial growth factor receptor inhibitors.
 INVENTOR(S): Seidelmann, Dieter; Krueger, Martin; Petrov, Orlin; Huth, Andreas; Thierauch, Karl-Heinz; Menrad, Andreas; Haberey, Martin
 PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
 SOURCE: PCT Int. Appl., 39 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-------------------|------------|
| WO 2001085715 | A2 | 20011115 | WO 2001-EP5264 | 20010509 |
| WO 2001085715 | A3 | 20020418 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10023492 | A1 | 20011122 | DE 2000-10023492 | 20000509 |
| US 2004224968 | A1 | 20041111 | US 2003-275584 | 20030509 |
| PRIORITY APPLN. INFO.: | | | DE 2000-10023492 | A 20000509 |
| | | | WO 2001-EP5264 | W 20010509 |
| OTHER SOURCE(S): | | | MARPAT 135:357941 | |
| GI | | | | |



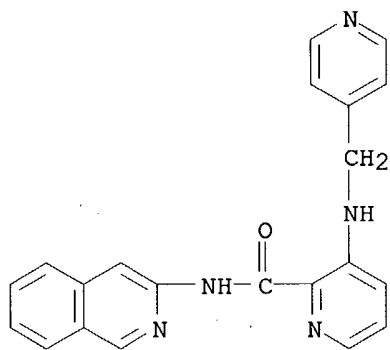
AB Title compds. [I; A = NR7; W = O, S, H2, NR8; Z = bond, NR10, N, alkyl, etc.; R1 = (substituted) alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl; R2 = (substituted) aryl, heteroaryl; R3-R6 = H, (substituted) alkoxy, alkyl, carboxyalkyl; X = alkylene; R7 = H, alkyl; R8, R10 = H, alkyl; D = N, CR3; E = N, CR4; F = N, CR5; G = N, R6], were prepared. Thus, 3-aminoisoquinoline in PhMe was treated with Me3Al in PhMe; after 10 min. Me 4-[(4-pyridyl)methyl]aminopyrimidine-5-carboxylate was added followed by heating at 120° to give 24% N-isoquinolin-3-yl 4-[(4-pyridyl)methyl]aminopyrimidine-5-carboxamide. The latter inhibited VEGFR II with IC50 = 100 nM.

IT 372512-44-2P 372512-48-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoheteroarylcarboxamides as vascular endothelial growth factor receptor inhibitors)

RN 372512-44-2 CAPLUS

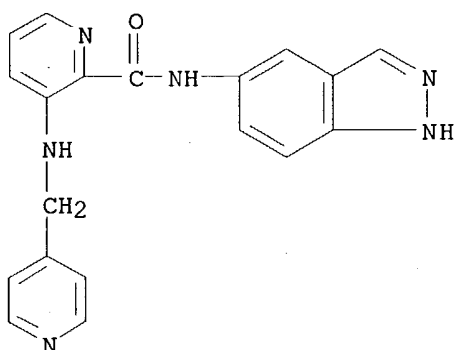
CN 2-Pyridinecarboxamide, N-3-isoquinolinyl-3-[(4-pyridinylmethyl)amino]-
(9CI) (CA INDEX NAME)



RN 372512-48-6 CAPLUS

CN 2-Pyridinecarboxamide, N-1H-indazol-5-yl-3-[(4-pyridinylmethyl)amino]-
(9CI) (CA INDEX NAME)

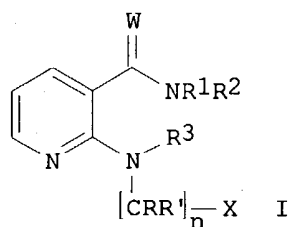
10/046,681



L8 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:565010 CAPLUS
DOCUMENT NUMBER: 135:137407
TITLE: Preparation of 2-aminonicotinamides as VEGF-receptor tyrosine kinase inhibitors
INVENTOR(S): Manley, Paul William; Bold, Guido
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2001055114 | A1 | 20010802 | WO 2001-EP835 | 20010125 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2001028499 | A5 | 20010807 | AU 2001-28499 | 20010125 |
| AU 771626 | B2 | 20040401 | | |
| BR 2001007805 | A | 20021022 | BR 2001-7805 | 20010125 |
| EP 1259487 | A1 | 20021127 | EP 2001-946854 | 20010125 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| JP 2003520853 | T2 | 20030708 | JP 2001-555056 | 20010125 |
| NZ 520005 | A | 20040227 | NZ 2001-520005 | 20010125 |
| NO 2002003218 | A | 20020916 | NO 2002-3218 | 20020702 |
| US 2003032656 | A1 | 20030213 | US 2002-181005 | 20020711 |
| US 6624174 | B2 | 20030923 | | |
| ZA 2002005988 | A | 20030728 | ZA 2002-5988 | 20020726 |
| PRIORITY APPLN. INFO.: | | | GB 2000-1930 | A 20000127 |
| | | | WO 2001-EP835 | W 20010125 |

OTHER SOURCE(S): MARPAT 135:137407
GI



AB The title compds. [I; n = 1-6; W = O, S; R1, R3 = H, alkyl, acyl; R2 = (un)substituted cycloalkyl, aryl, mono- or bicyclic heteroaryl comprising one or more ring N atoms and 0-2 heteroatoms selected from O and S; R, R' = H, alkyl; X = (un)substituted aryl, mono- or bicyclic heteroaryl comprising one or more ring N atoms and 0-2 heteroatoms selected from O and S] and their pharmaceutically acceptable salts, useful for therapy of a disease which responds to an inhibition of the VEGF-receptor tyrosine kinase activity (such as neoplastic disease), were prepared and formulated. Thus, amidation of 3-aminobenzotrifluoride with 2-chloronicotinoyl chloride followed by reacting 4-pyridineethanamine with the resulting carboxamide afforded I [n = 2; R, R' = H; X = 4-pyridyl; W = O; R1, R3 = H; R2 = 3-(F3C)C6H4].

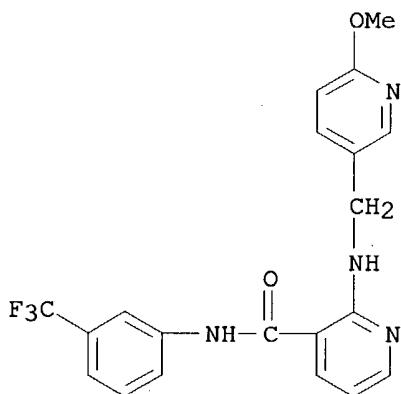
IT **352227-59-9P 352227-60-2P 352227-77-1P**
352227-82-8P 352227-83-9P 352227-84-0P
352227-88-4P 352227-89-5P 352227-93-1P
352227-97-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of 2-aminonicotinamides as VEGF-receptor tyrosine kinase inhibitors)

RN 352227-59-9 CAPLUS

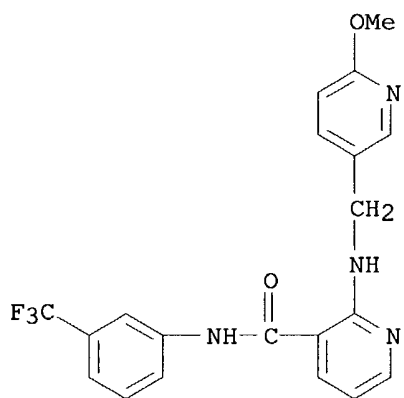
CN 3-Pyridinecarboxamide, 2-[[[6-methoxy-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 352227-60-2 CAPLUS

CN 3-Pyridinecarboxamide, 2-[[[6-methoxy-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]-, dihydrochloride (9CI) (CA INDEX NAME)

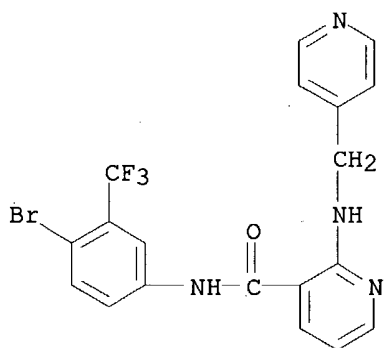
10/046,681



●2 HCl

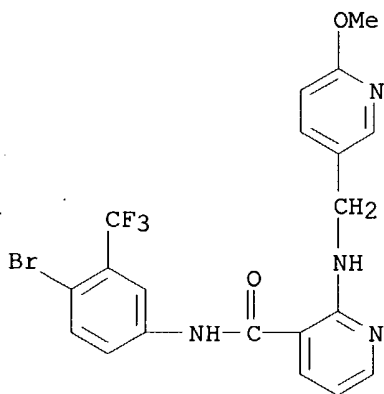
RN 352227-77-1 CAPLUS

CN 3-Pyridinecarboxamide, N-[4-bromo-3-(trifluoromethyl)phenyl]-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)



RN 352227-82-8 CAPLUS

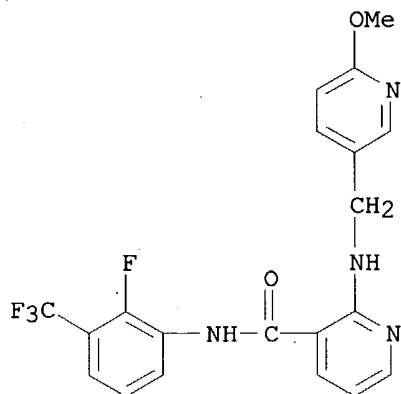
CN 3-Pyridinecarboxamide, N-[4-bromo-3-(trifluoromethyl)phenyl]-2-[[6-methoxy-3-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)



10/046,681

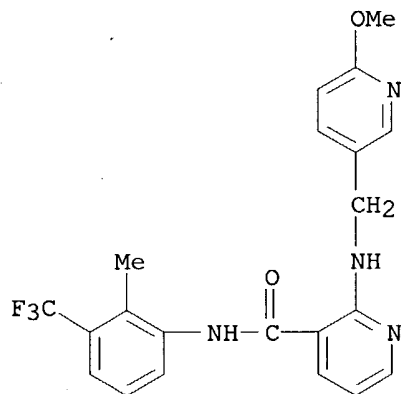
RN 352227-83-9 CAPLUS

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RN 352227-84-0 CAPLUS

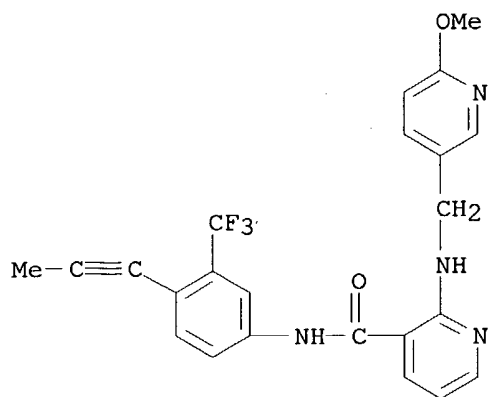
CN 3-Pyridinecarboxamide, 2-[[6-methoxy-3-pyridinyl)methyl]amino]-N-[2-methyl-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 352227-88-4 CAPLUS

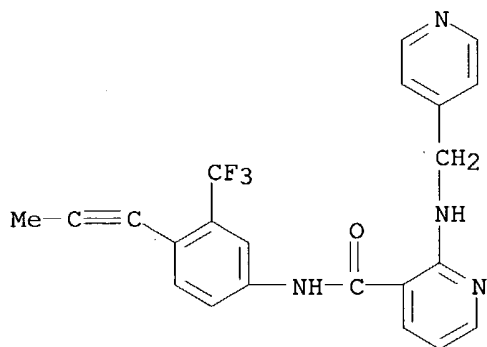
CN 3-Pyridinecarboxamide, 2-[[6-methoxy-3-pyridinyl)methyl]amino]-N-[4-(1-propynyl)-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

10/046,681



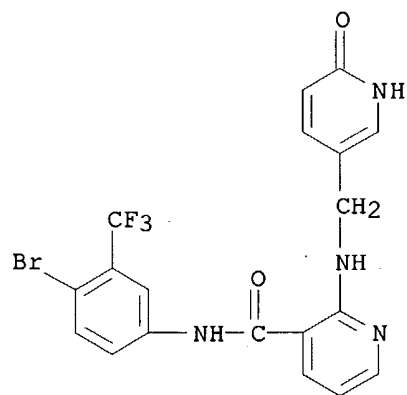
RN 352227-89-5 CAPLUS

CN 3-Pyridinecarboxamide, N-[4-(1-propynyl)-3-(trifluoromethyl)phenyl]-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)



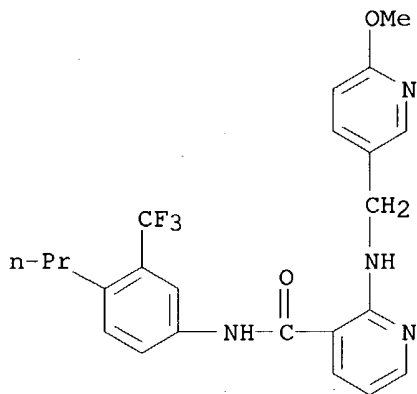
RN 352227-93-1 CAPLUS

CN 3-Pyridinecarboxamide, N-[4-bromo-3-(trifluoromethyl)phenyl]-2-[[1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)



RN 352227-97-5 CAPLUS

CN 3-Pyridinecarboxamide, 2-[[6-methoxy-3-pyridinyl)methyl]amino]-N-[4-propyl-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

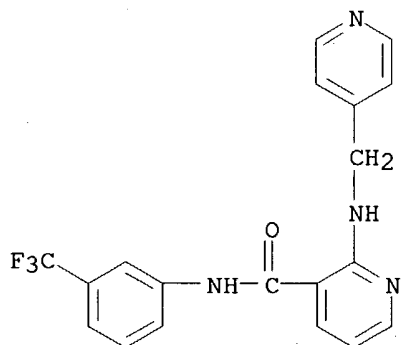


IT 352227-57-7P 352227-58-8P 352227-61-3P
 352227-62-4P 352227-63-5P 352227-64-6P
 352227-65-7P 352227-69-1P 352227-70-4P
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 352228-04-7P 352228-05-8P 352228-06-9P
 352228-07-0P 352228-08-1P 352228-09-2P
 352228-10-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of 2-aminonicotinamides as VEGF-receptor tyrosine kinase inhibitors)

RN 352227-57-7 CAPLUS

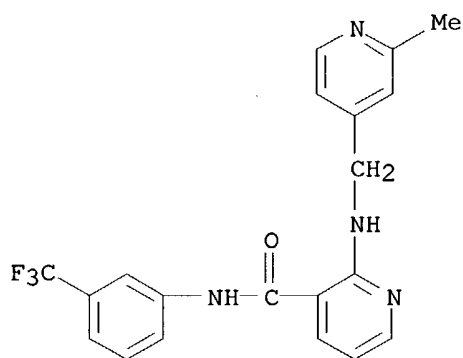
CN 3-Pyridinecarboxamide, 2-[(4-pyridinylmethyl)amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 352227-58-8 CAPLUS

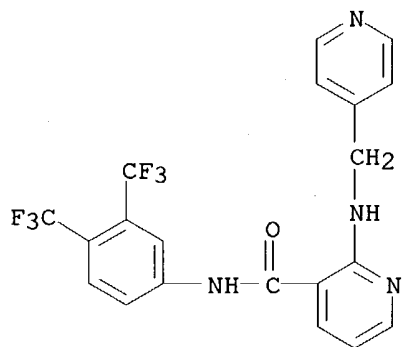
CN 3-Pyridinecarboxamide, 2-[[2-methyl-4-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

10/046,681



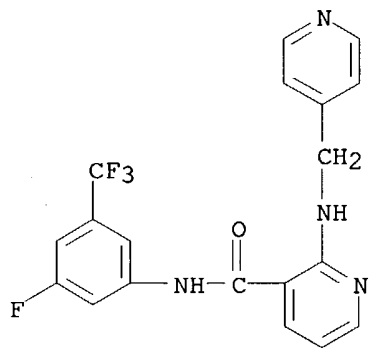
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CN 3-Pyridinecarboxamide, N-[3,4-bis(trifluoromethyl)phenyl]-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)



RN 352227-62-4 CAPLUS

CN 3-Pyridinecarboxamide, N-[3-fluoro-5-(trifluoromethyl)phenyl]-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

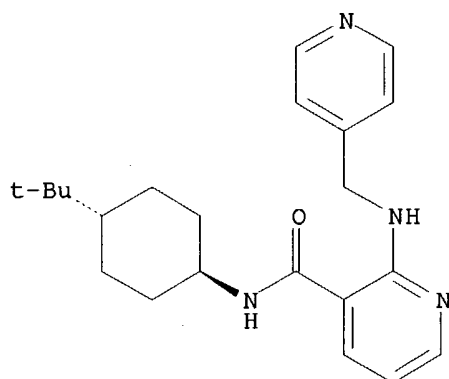


RN 352227-63-5 CAPLUS

CN 3-Pyridinecarboxamide, N-[trans-4-(1,1-dimethylethyl)cyclohexyl]-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

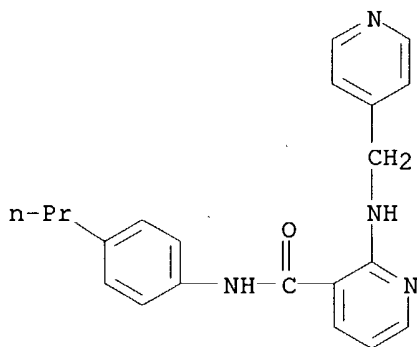
Relative stereochemistry.

10/046,681



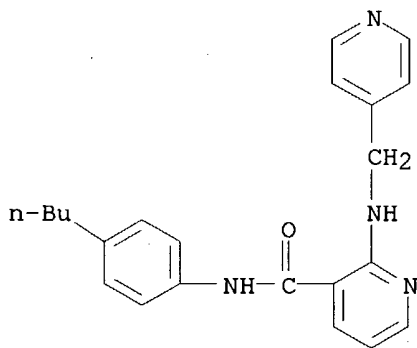
RN 352227-64-6 CAPLUS

CN 3-Pyridinecarboxamide, N-(4-propylphenyl)-2-[(4-pyridinylmethyl)amino]-
(9CI) (CA INDEX NAME)



RN 352227-65-7 CAPLUS

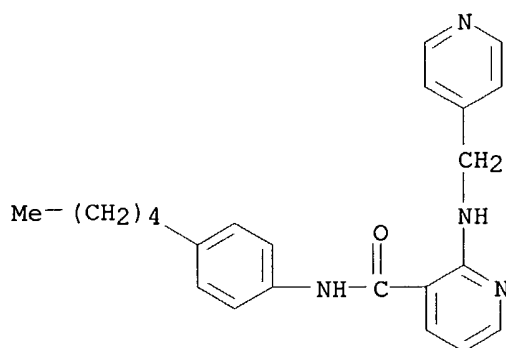
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RN 352227-69-1 CAPLUS

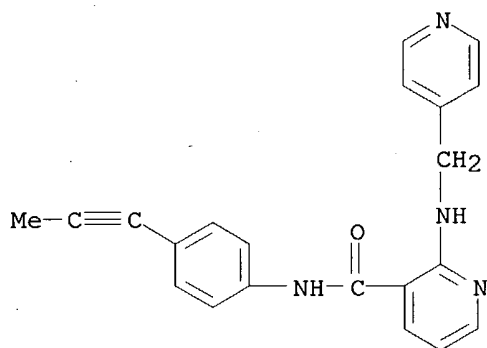
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10/046,681



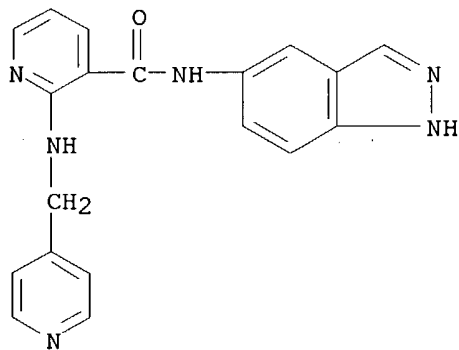
RN 352227-70-4 CAPLUS

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RN 352227-71-5 CAPLUS

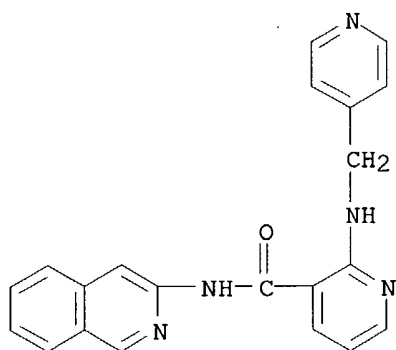
CN 3-Pyridinecarboxamide, N-1H-indazol-5-yl-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)



RN 352227-72-6 CAPLUS

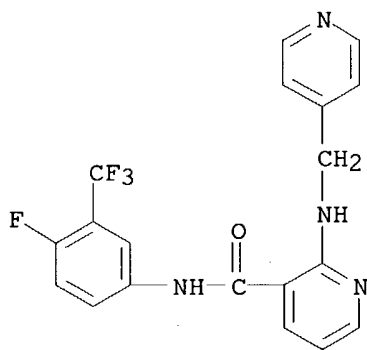
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10/046,681



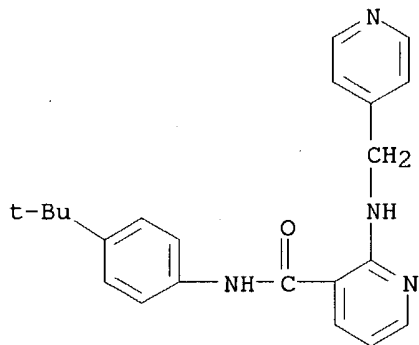
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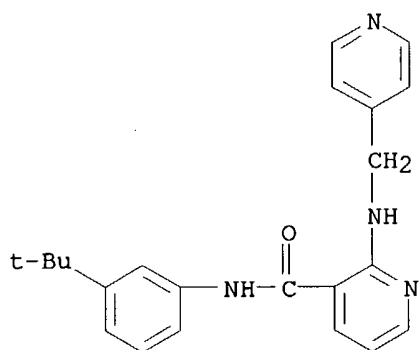
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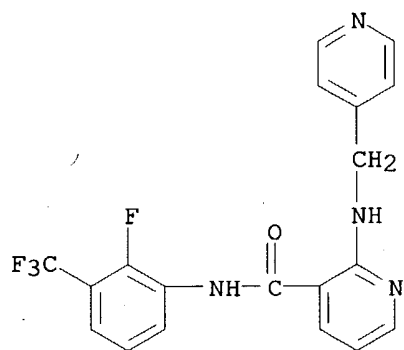
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10/046,681



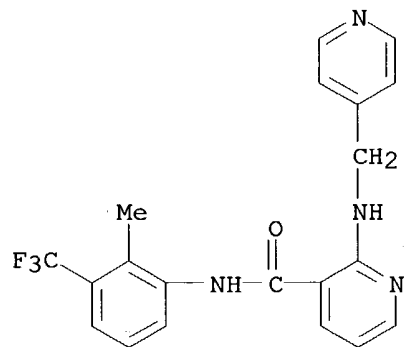
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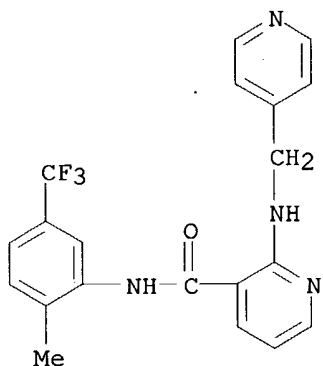
CN 3-Pyridinecarboxamide, N-[2-methyl-3-(trifluoromethyl)phenyl]-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)



RN 352227-80-6 CAPLUS

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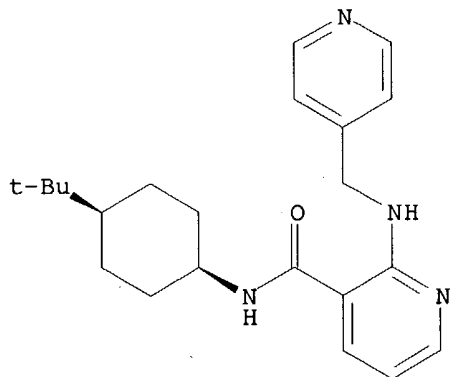
10/046,681



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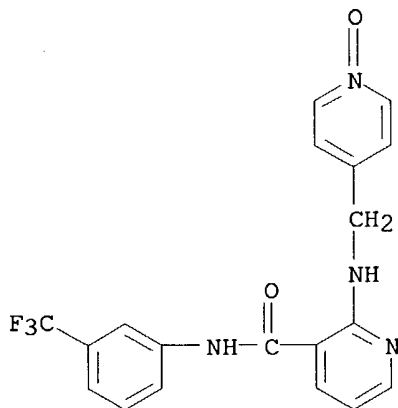
CN 3-Pyridinecarboxamide, N-[cis-4-(1,1-dimethylethyl)cyclohexyl]-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 352227-85-1 CAPLUS

CN 3-Pyridinecarboxamide, 2-[[[(1-oxido-4-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

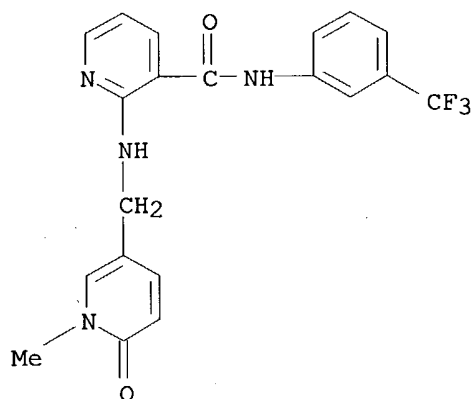


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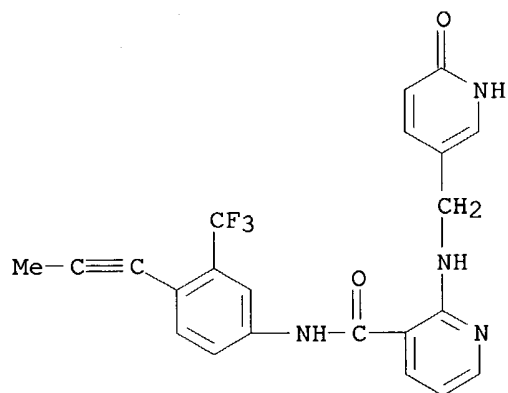
10/046,681

pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



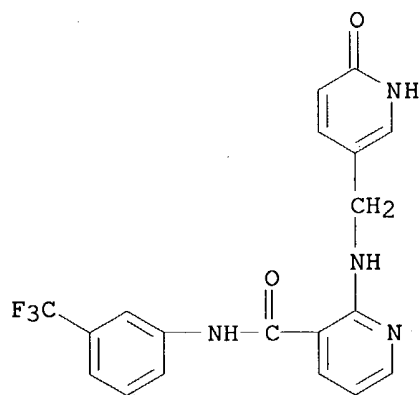
RN 352227-90-8 CAPLUS

CN 3-Pyridinecarboxamide, 2-[[[1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-(1-propynyl)-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 352227-91-9 CAPLUS

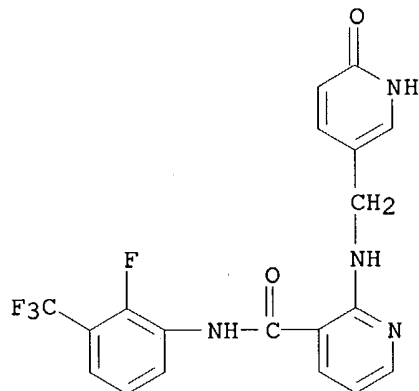
CN 3-Pyridinecarboxamide, 2-[[[1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



10/046,681

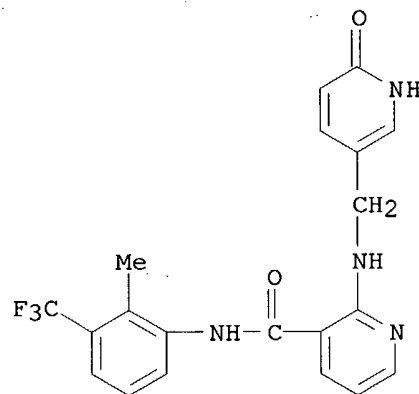
RN 352227-94-2 CAPLUS

CN 3-Pyridinecarboxamide, 2-[[[1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[2-fluoro-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 352227-95-3 CAPLUS

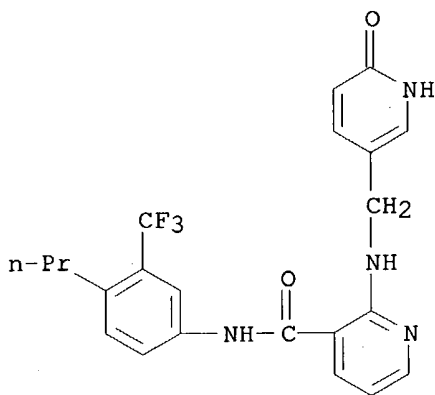
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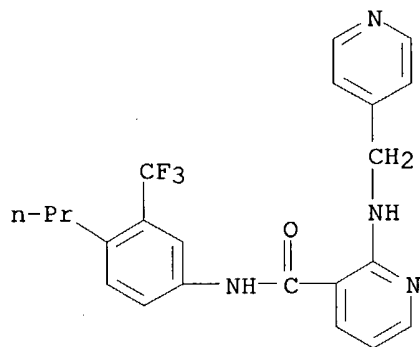
CN 3-Pyridinecarboxamide, 2-[[[1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-propyl-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

10/046,681



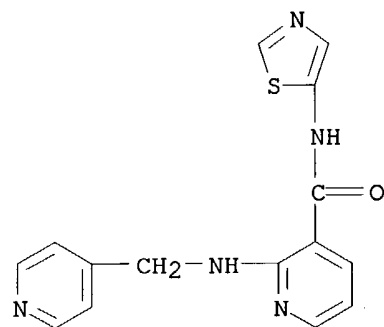
RN 352227-98-6 CAPLUS

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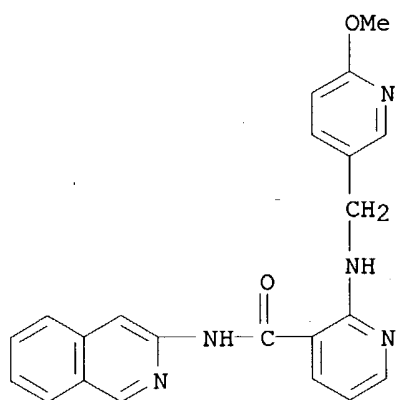
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RN 352228-01-4 CAPLUS

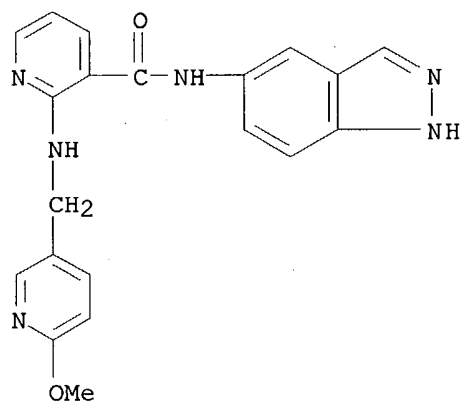
CN 3-Pyridinecarboxamide, N-3-isoquinolinyl-2-[[(6-methoxy-3-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)

10/046,681



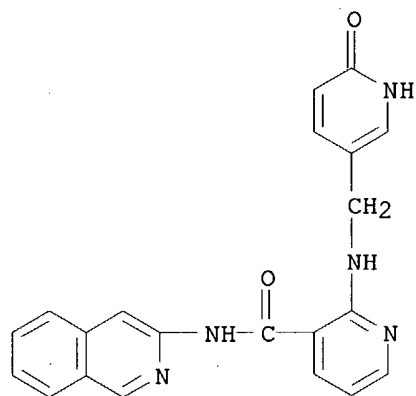
RN 352228-02-5 CAPLUS

CN 3-Pyridinecarboxamide, N-1H-indazol-5-yl-2-[[(6-methoxy-3-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)



RN 352228-03-6 CAPLUS

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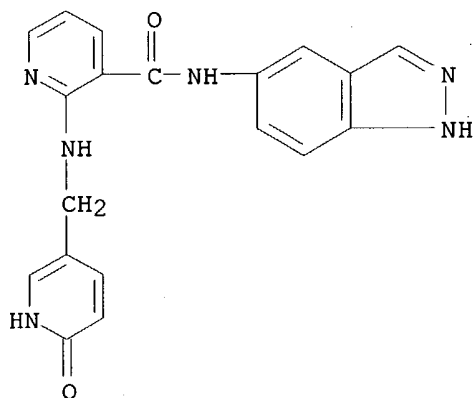


RN 352228-04-7 CAPLUS

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10/046,681

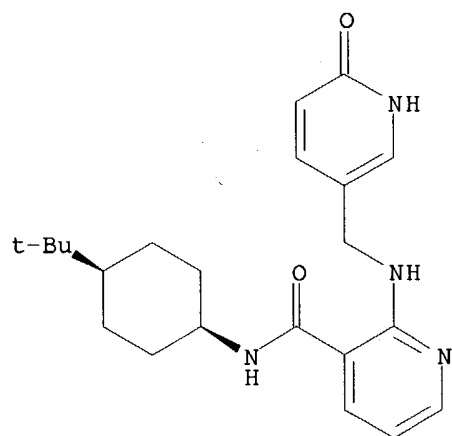
1H-indazol-5-yl- (9CI) (CA INDEX NAME)



RN 352228-05-8 CAPLUS

CN 3-Pyridinecarboxamide, 2-[[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[cis-4-(1,1-dimethylethyl)cyclohexyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

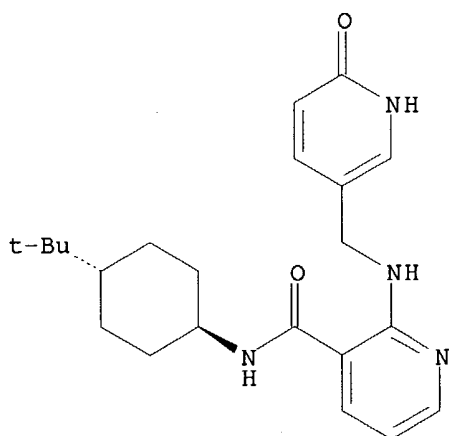


RN 352228-06-9 CAPLUS

CN 3-Pyridinecarboxamide, 2-[[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[trans-4-(1,1-dimethylethyl)cyclohexyl]- (9CI) (CA INDEX NAME)

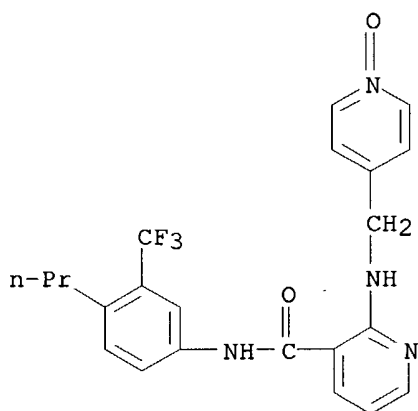
Relative stereochemistry.

10/046,681



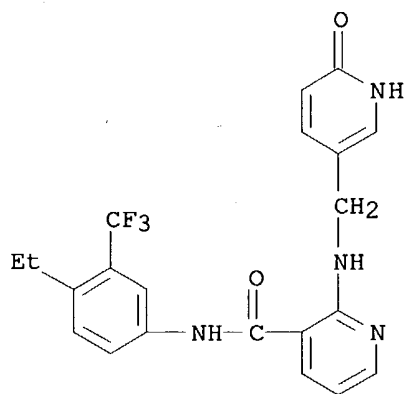
RN 352228-07-0 CAPLUS

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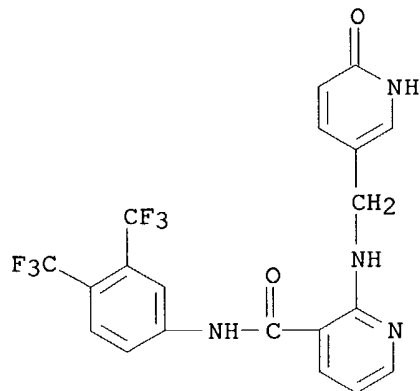
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10/046,681

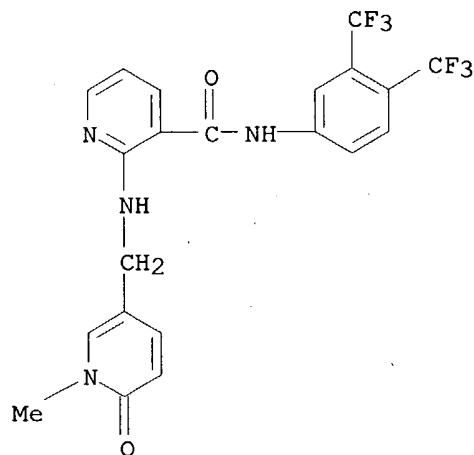
RN 352228-09-2 CAPLUS

CN 3-Pyridinecarboxamide, N-[3,4-bis(trifluoromethyl)phenyl]-2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)



RN 352228-10-5 CAPLUS

CN 3-Pyridinecarboxamide, N-[3,4-bis(trifluoromethyl)phenyl]-2-[[(1,6-dihydro-1-methyl-6-oxo-3-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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MISSING OPERATOR L9 1-3

The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

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L9 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:950057 CAPLUS

DOCUMENT NUMBER: 140:16647

TITLE: Preparation of 2-aminopyridine-3-carboxamides as remedies for angiogenesis mediated diseases

applied

10/046,681

INVENTOR(S): Askew, Benny; Adams, Jeffrey; Booker, Shon; Chen, Guoqing; Dipietro, Lucian V.; Elbaum, Daniel; Germain, Julie; Geuns-Meyer, Stephanie D.; Habgood, Gregory J.; Handley, Michael; Huang, Qi; Kim, Tae-seong; Li, Aiwen; Nishimura, Nobuko; Nomak, Rana; Patel, Vinod F.; Riahi, Babak; Kim, Joseph L.; Xi, Ning; Yang, Kevin; Yuan, Chester Chenguang

PATENT ASSIGNEE(S): Amgen Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 252 pp., Cont.-in-part of U.S. Ser. No. 46,681.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2003225106 | A1 | 20031204 | US 2002-197974 | 20020717 |
| US 2003125339 | A1 | 20030703 | US 2002-46681 | 20020110 |
| ZA 2003005197 | A | 20040319 | ZA 2003-5197 | 20030704 |
| WO 2004007458 | A1 | 20040122 | WO 2003-US22417 | 20030715 |

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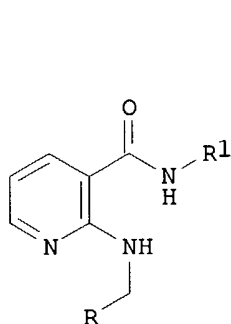
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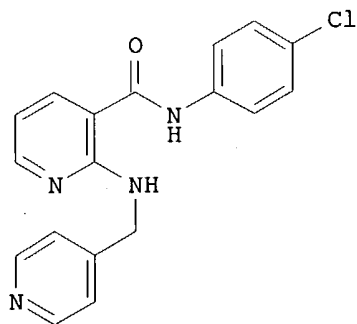
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| US 2001-261339P | P | 20010112 |
| US 2001-323764P | P | 20010919 |
| US 2002-46681 | A2 | 20020110 |
| US 2002-197974 | A | 20020717 |

OTHER SOURCE(S): MARPAT 140:16647

GI



I



II

AB The title compds. [I; R = (un)substituted 4-pyridyl, 2-pyridyl, 4-pyrimidinyl, 4-quinolyl, etc.; R₁ = (un)substituted aryl, cycloalkyl, 5-6 membered heteroaryl, 9-10 membered bicyclic and 11-14 membered tricyclic heterocyclyl], which are effective for prophylaxis and treatment of diseases and other maladies or conditions involving, cancer and the

like, were prepared. Thus, the title compound II was prepared from 2-aminonicotinic acid, 4-chloroaniline, and 4-pyridinecarboxaldehyde. The compds. I showed inhibition of KDR kinase at < 50 μ M. Many compds. I inhibited VEGF-stimulated HUVEC proliferation at a level below 50 nM. Pharmaceutical composition comprising the compound I is claimed.

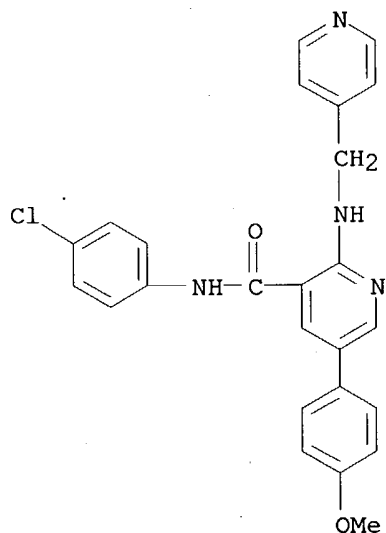
IT **453561-26-7P 453561-87-0P**, (S)-N-[3-(Pyrrolidin-2-ylmethoxy)-4-pentafluoroethylphenyl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide **453561-89-2P**, (R)-N-[3-(Pyrrolidin-2-ylmethoxy)-4-pentafluoroethylphenyl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide **453562-48-6P 453563-13-8P 453563-27-4P 453563-62-7P 453563-68-3P 453563-72-9P 453564-11-9P 629650-34-6P 629650-82-4P 629650-93-7P 629651-00-9P 629651-35-0P 629651-39-4P 629651-49-6P 629651-63-4P 629651-81-6P 629651-90-7P 629651-98-5P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-aminopyridine-3-carboxamides for treating angiogenesis mediated diseases)

RN 453561-26-7 CAPLUS

CN 3-Pyridinecarboxamide, N-(4-chlorophenyl)-5-(4-methoxyphenyl)-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

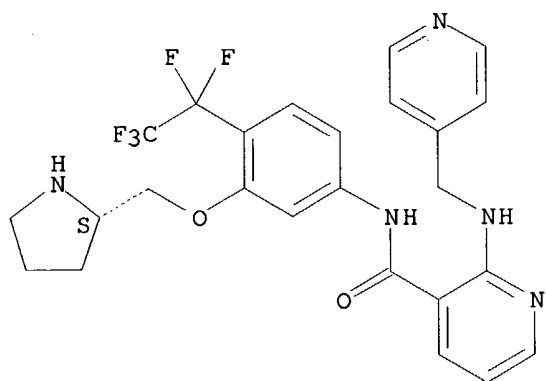


RN 453561-87-0 CAPLUS

CN 3-Pyridinecarboxamide, N-[4-(pentafluoroethyl)-3-[(2S)-2-pyrrolidinylmethoxy]phenyl]-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

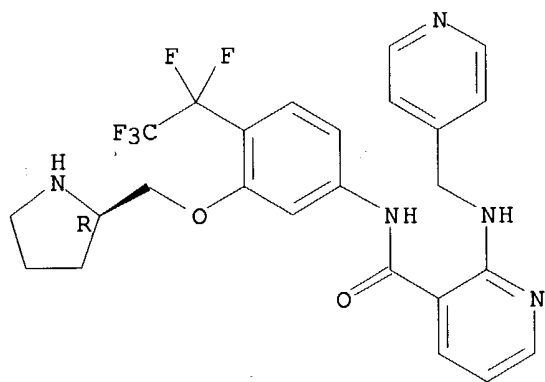
10/046,681



RN 453561-89-2 CAPLUS

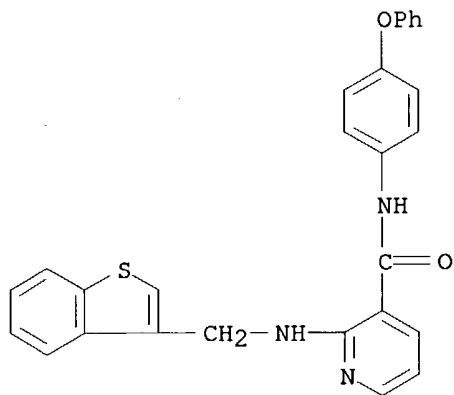
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Absolute stereochemistry.



RN 453562-48-6 CAPLUS

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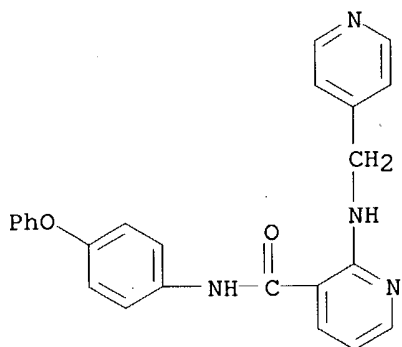


RN 453563-13-8 CAPLUS

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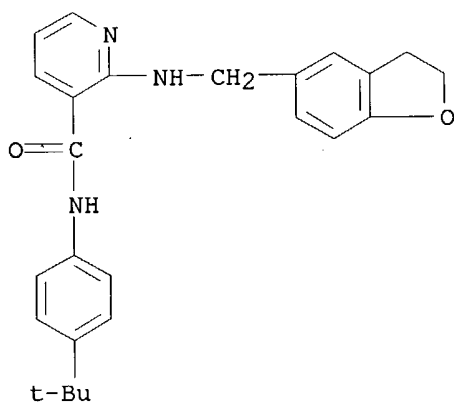
10/046,681

(9CI) (CA INDEX NAME)



RN 453563-27-4 CAPLUS

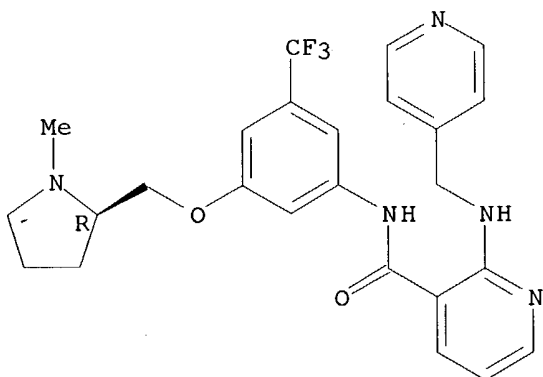
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RN 453563-62-7 CAPLUS

CN 3-Pyridinecarboxamide, N-[3-[[[(2R)-1-methyl-2-pyrrolidinyl]methoxy]-5-(trifluoromethyl)phenyl]-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

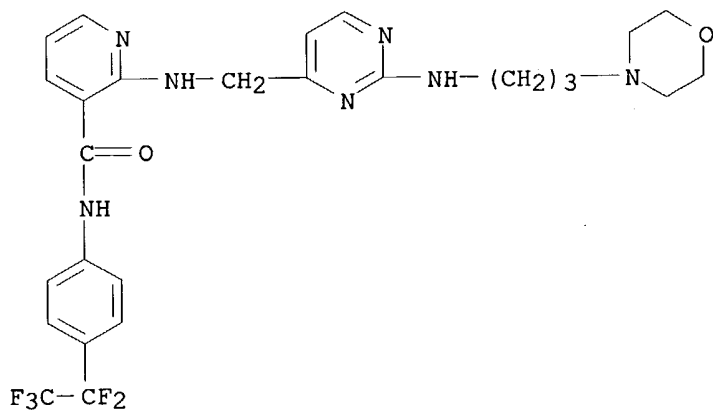
Absolute stereochemistry.



10/046,681

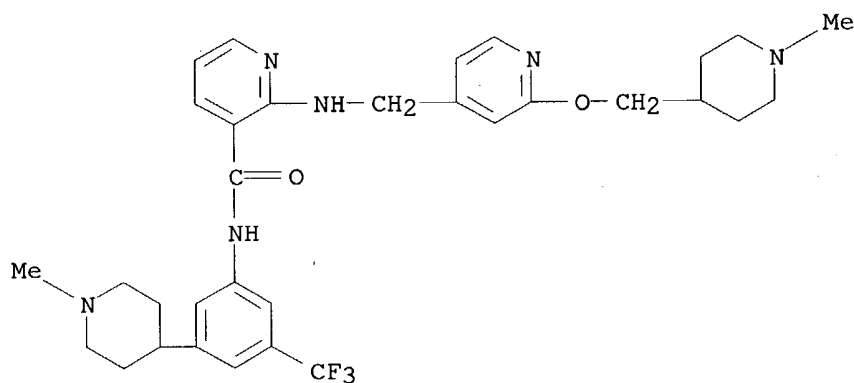
RN 453563-68-3 CAPLUS

CN 3-Pyridinecarboxamide, 2-[[[2-[[3-(4-morpholinyl)propyl]amino]-4-pyrimidinyl]methyl]amino]-N-[4-(pentafluoroethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 453563-72-9 CAPLUS

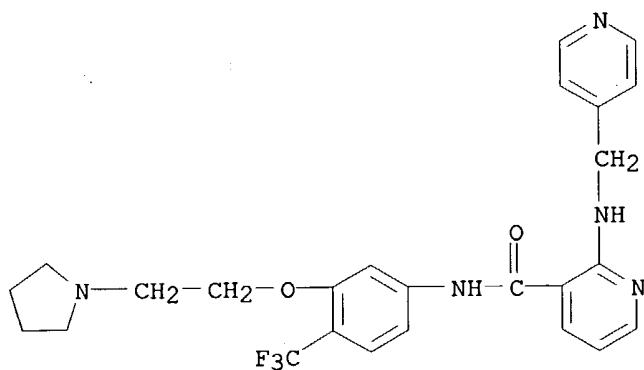
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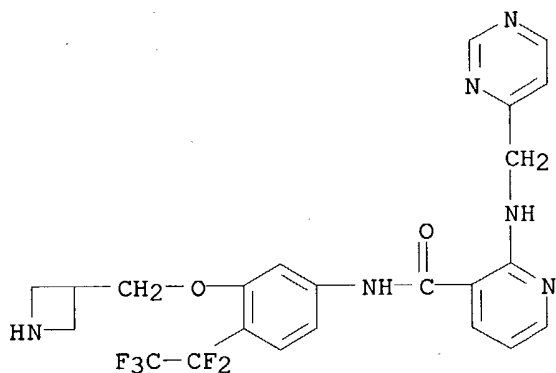
RN 453564-11-9 CAPLUS

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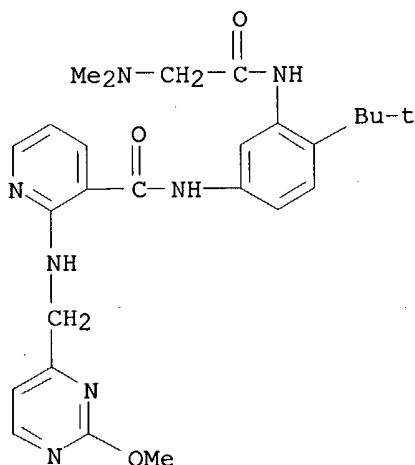
10/046,681



RN 629650-34-6 CAPLUS
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RN 629650-82-4 CAPLUS
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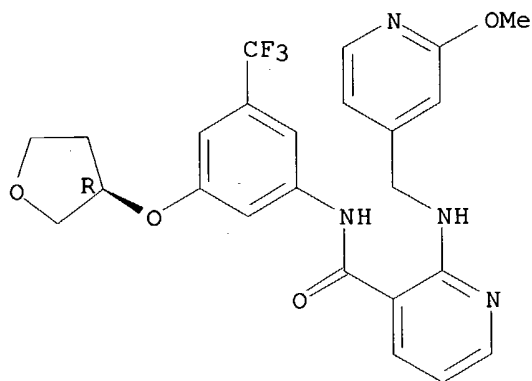


10/046,681

RN 629650-93-7 CAPLUS

CN 3-Pyridinecarboxamide, 2-[[[2-methoxy-4-pyridinyl)methyl]amino]-N-[3-
[[[(3R)-tetrahydro-3-furanyl]oxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA
INDEX NAME)

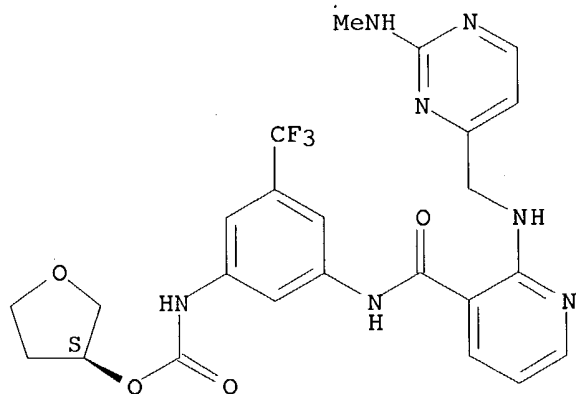
Absolute stereochemistry.



RN 629651-00-9 CAPLUS

CN Carbamic acid, [3-[[[2-[[[2-(methylamino)-4-pyrimidinyl]methyl]amino]-3-
pyridinyl]carbonyl]amino]-5-(trifluoromethyl)phenyl]-,
(3S)-tetrahydro-3-furanyl ester (9CI) (CA INDEX NAME)

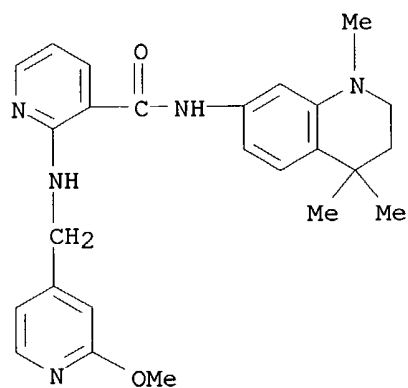
Absolute stereochemistry.



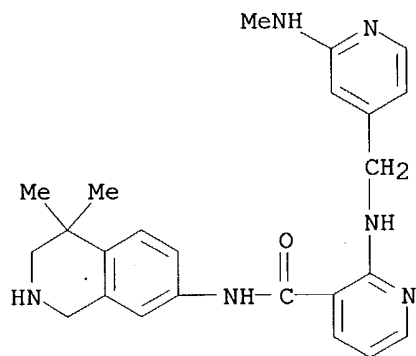
RN 629651-35-0 CAPLUS

CN 3-Pyridinecarboxamide, 2-[[[2-methoxy-4-pyridinyl)methyl]amino]-N-(1,2,3,4-
tetrahydro-1,4,4-trimethyl-7-quinolinyl)- (9CI) (CA INDEX NAME)

10/046,681

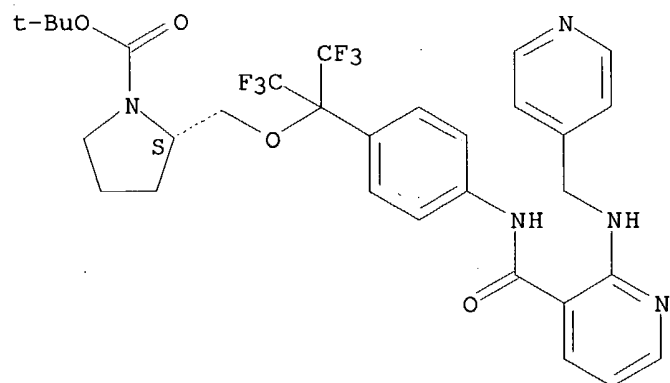


RN 629651-39-4 CAPLUS
CN 3-Pyridinecarboxamide, 2-[[[2-(methylamino)-4-pyridinyl]methyl]amino]-N-(1,2,3,4-tetrahydro-4,4-dimethyl-7-isoquinolinyl)- (9CI) (CA INDEX NAME)



RN 629651-49-6 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 2-[[[2,2,2-trifluoro-1-[4-[[[2-[(4-pyridinylmethyl)amino]-3-pyridinyl]carbonyl]amino]phenyl]-1-(trifluoromethyl)ethoxy]methyl]-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

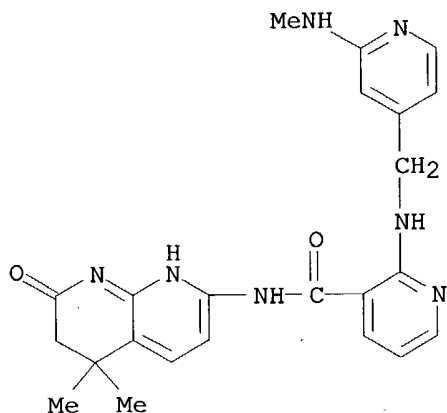
Absolute stereochemistry.



RN 629651-63-4 CAPLUS

10/046,681

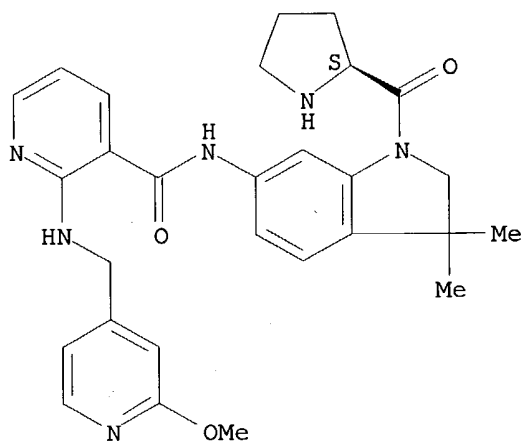
CN 3-Pyridinecarboxamide, 2-[[[2-(methylamino)-4-pyridinyl]methyl]amino]-N-(1,5,6,7-tetrahydro-5,5-dimethyl-7-oxo-1,8-naphthyridin-2-yl)- (9CI) (CA INDEX NAME)



RN 629651-81-6 CAPLUS

CN 3-Pyridinecarboxamide, N-[2,3-dihydro-3,3-dimethyl-1-[(2S)-2-pyrrolidinylcarbonyl]-1H-indol-6-yl]-2-[[[2-methoxy-4-pyridinyl]methyl]amino]- (9CI) (CA INDEX NAME)

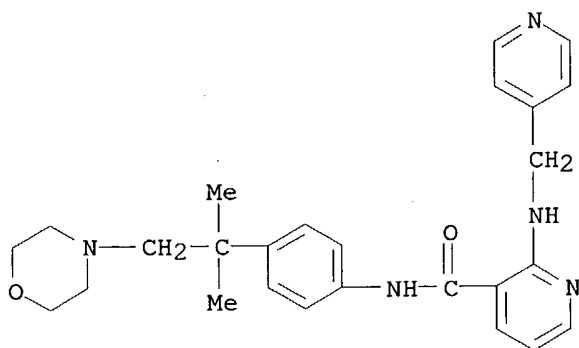
Absolute stereochemistry.



RN 629651-90-7 CAPLUS

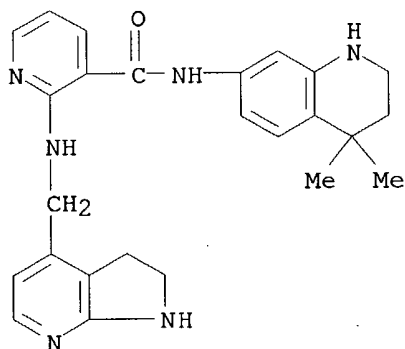
CN 3-Pyridinecarboxamide, N-[4-[1,1-dimethyl-2-(4-morpholinyl)ethyl]phenyl]-2-[[[4-pyridinylmethyl]amino]- (9CI) (CA INDEX NAME)

10/046,681



RN 629651-98-5 CAPLUS

CN 3-Pyridinecarboxamide, 2-[[[2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-4-yl)methyl]amino]-N-(1,2,3,4-tetrahydro-4,4-dimethyl-7-quinolinyl)- (9CI)
(CA INDEX NAME)



L9 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:868928 CAPLUS

DOCUMENT NUMBER: 137:352900

TITLE: Selective anthranilamide pyridine amides as inhibitors of VEGFR-2 and VEGFR-3

INVENTOR(S): Ernst, Alexander; Huth, Andreas; Krueger, Martin; Thierauch, Karl-Heinz; Menrad, Andreas; Haberey, Martin

PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany

SOURCE: PCT Int. Appl., 115 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

date not good

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2002090352 | A2 | 20021114 | WO 2002-EP4924 | 20020503 |
| WO 2002090352 | A3 | 20030501 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,

UG, US, UZ, VN, YU, ZA, ZM, ZW
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 GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
 GN, GQ, GW, ML, MR, NE, SN, TD, TG

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|-------------|----|----------|------------------|----------|
| DE 10123574 | A1 | 20021128 | DE 2001-10123574 | 20010508 |
| DE 10125294 | A1 | 20021121 | DE 2001-10125294 | 20010515 |
| DE 10164590 | A1 | 20030710 | DE 2001-10164590 | 20011221 |
| EP 1392680 | A2 | 20040303 | EP 2002-735333 | 20020503 |

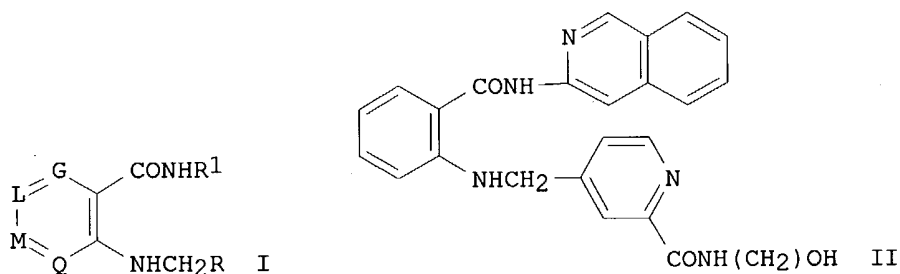
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

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|---------------|----|----------|----------------|----------|
| BR 2002009485 | A | 20040706 | BR 2002-9485 | 20020503 |
| JP 2004528379 | T2 | 20040916 | JP 2002-587431 | 20020503 |

PRIORITY APPLN. INFO.:

| | | |
|------------------|---|----------|
| DE 2001-10123574 | A | 20010508 |
| DE 2001-10125294 | A | 20010515 |
| DE 2001-10164590 | A | 20011221 |
| WO 2002-EP4924 | W | 20020503 |

OTHER SOURCE(S): MARPAT 137:352900
 GI



AB Title compds. I [G, L, M, Q = N, (un)substituted CH, ≤1 of them being N; R = (un)substituted N heterocycle; R¹ = (un)substituted alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl] were prepared I are inhibitors of VEGFR-2 and VEGFR-3 and are used as medicaments for treating diseases that are caused by persistent angiogenesis, such as psoriasis, Kaposi's sarcoma, restenosis, such as e.g. stent-induced restenosis, endometriosis, Crohn's disease, Hodgkin's disease, leukemia, arthritis, such as rheumatoid arthritis, hemangioma, angiofibromatosis, in eye diseases such as diabetic retinopathy, neovascular glaucoma, in kidney diseases such as glomerulonephritis, diabetic nephropathy, malign nephrosclerosis, thrombic micro-angiopathic syndrome, transplant rejection and glomerulopathy, in fibrotic diseases such as hepatic cirrhosis, mesangial-cell proliferative diseases, arteriosclerosis, damage to the nerve tissue and inhibition of the re-occlusion of vessels after balloon catheter treatment, in vessel prosthetics or after the use of mech. devices for keeping vessels open, e.g. stents, as immunosuppressants, to support wound healing without scars and in cases of age spots and contact dermatitis. I can also be used as inhibitors of VEGFR-3 in lymphangiogenesis for hyperplastic and dysplastic changes in the lymphatic system. Thus, 2-amino-N-isoquinolin-3-ylbenzamide was treated with 2-bromo-5-pyridinecarboxaldehyde, followed by carboxylation and amidation to give the amide II. II had IC₅₀ for inhibition of VEGFR-2 of 40 nM and for inhibition of cytochrome 450 isoenzyme 2C9 of 2.9 μM.

IT 474799-26-3P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

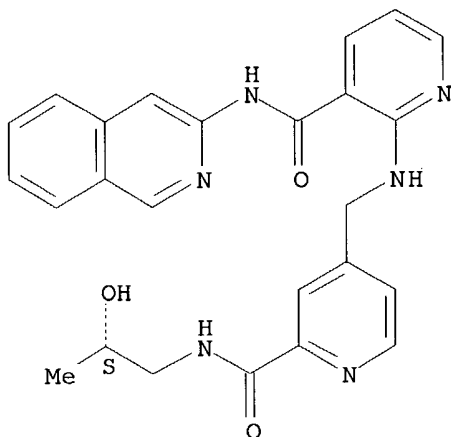
10/046,681

(preparation of isoquinolinylcarbamoylphenylaminomethylpyridinecarboxamides
as VEGFR-2 and VEGFR-3 inhibitors)

RN 474799-26-3 CAPLUS

CN 2-Pyridinecarboxamide, N-[(2S)-2-hydroxypropyl]-4-[[[3-[(3-
isoquinolinylamino)carbonyl]-2-pyridinyl]amino]methyl]- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.



L9 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:658116 CAPLUS

DOCUMENT NUMBER: 137:201332

TITLE: Preparation of heterocyclylalkylamine derivatives as
remedies for angiogenesis mediated diseases

INVENTOR(S): Chen, Guoqing; Adams, Jeffrey; Bemis, Jean; Booker,
Shon; Cai, Guolin; Croghan, Michael; Dipietro, Lucian;
Dominguez, Celia; Elbaum, Daniel; Germain, Julie;
Geuns-meyer, Stephanie; Handley, Michael; Huang, Qi;
Kim, Joseph L.; Kim, Tae-seong; Kiselyov, Alexander;
Ouyang, Xiaohu; Patel, Vinod F.; Smith, Leon M.; Stec,
Markian; Tasker, Andrew; Xi, Ning; Xu, Shimin; Yuan,
Chester Chenguang

PATENT ASSIGNEE(S): Amgen Inc., USA

SOURCE: PCT Int. Appl., 502 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

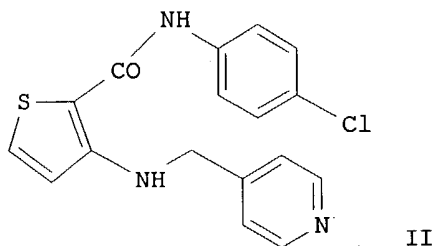
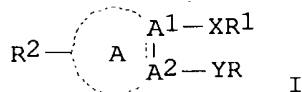
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2002066470 | A1 | 20020829 | WO 2002-US743 | 20020111 |
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| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, | | | |

applicants

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 US 2003125339 A1 20030703 US 2002-46681 20020110
 BR 2002006435 A 20030923 BR 2002-6435 20020111
 EP 1358184 A1 20031105 EP 2002-717325 20020111
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 EE 200300324 A 20031215 EE 2003-324 20020111
 JP 2004531484 T2 20041014 JP 2002-565984 20020111
 ZA 2003005197 A 20040319 ZA 2003-5197 20030704
 NO 2003003181 A 20030911 NO 2003-3181 20030711
 PRIORITY APPLN. INFO.: US 2001-261339P P 20010112
 US 2001-323764P P 20010919
 US 2002-46681 A 20020110
 WO 2002-US743 W 20020111
 OTHER SOURCE(S): MARPAT 137:201332
 GI



AB Title compds. [I; A1, A2 independently = C, N; A = 5-, or 6-membered partially saturated heterocyclyl, 5-, or 6-membered heterocyclyl, 9-, or 10-membered fused partially saturated heterocyclyl, 9-, 10-, or 11-membered fused heteroaryl, naphthyl, 4-, 5-, or 6-membered cycloalkenyl; X = C:ZNR3, C:ZN(R3)R4; Z = O, S; Y = N:CH, NR5(CR6R7), R8N(R5)(CR6R7), NR5(CR6R7)R8; R = 5-, or 6-membered (un)substituted heterocyclyl, 9-, 10-, 11-membered heterocyclyl; R1 = 6-10-membered (un)substituted aryl, 5-, or 6-membered (un)substituted heterocyclyl, 9-11 membered (un)substituted fused heterocyclyl, cycloalkyl, cycloalkenyl; R2 = H, halo, oxo, SH, COOH, CHO; R3 = H, alkyl, 5-, or 6-membered heterocyclyl; R4 = alkylenyl, alkenylenyl, alkynylenyl; R5 = H, alkyl, aralkyl, C6H5; R6, R7 independently = H, halo, CN, alkyl; R6R7 = cycloalkyl; R8 = alkylenyl; etc.] are prepared and are effective for prophylaxis and treatment of diseases, such as angiogenesis mediated diseases. The invention encompasses novel compds., analogs, prodrugs and pharmaceutically acceptable derivs. thereof, pharmaceutical compns. and methods for prophylaxis and treatment of diseases and other maladies or conditions involving, cancer and the like. The subject invention also relates to processes for making such compds. as well as to intermediates useful in

10/046,681

such processes. Thus, the title compound II was prepared from Me 3-amino-2-thiophenecarboxylate, 4-chloroaniline, and 4-pyridine carboxaldehyde via coupling reaction.

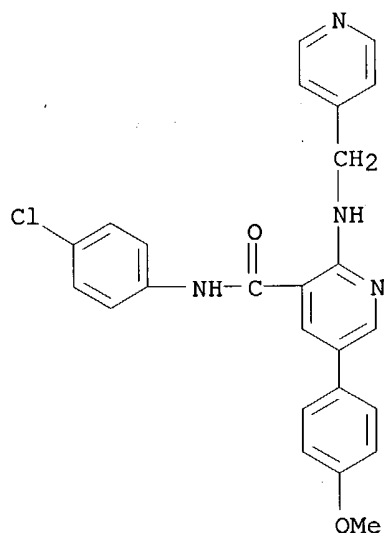
IT **453561-26-7P 453561-87-0P**, (S)-N-[3-(Pyrrolidin-2-ylmethoxy)-4-pentafluoroethylphenyl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide **453561-89-2P**, (R)-N-[3-(Pyrrolidin-2-ylmethoxy)-4-pentafluoroethylphenyl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide **453562-48-6P 453563-13-8P 453563-27-4P 453563-62-7P 453563-68-3P 453563-72-9P 453564-11-9P 453564-46-0P 453564-69-7P 453564-89-1P 453564-94-8P 453564-98-2P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of heterocyclalkylamine derivs. as remedies for angiogenesis mediated diseases)

RN 453561-26-7 CAPLUS

CN 3-Pyridinecarboxamide, N-(4-chlorophenyl)-5-(4-methoxyphenyl)-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

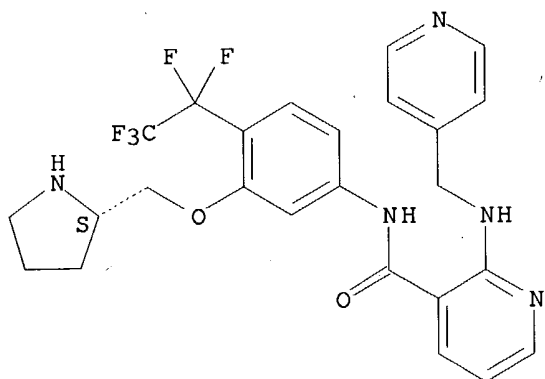


RN 453561-87-0 CAPLUS

CN 3-Pyridinecarboxamide, N-[4-(pentafluoroethyl)-3-[(2S)-2-pyrrolidinylmethoxy]phenyl]-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

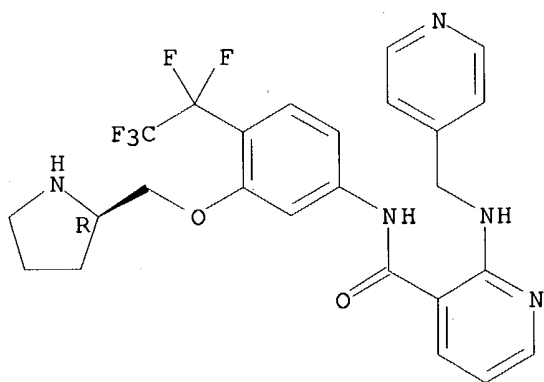
10/046,681



RN 453561-89-2 CAPLUS

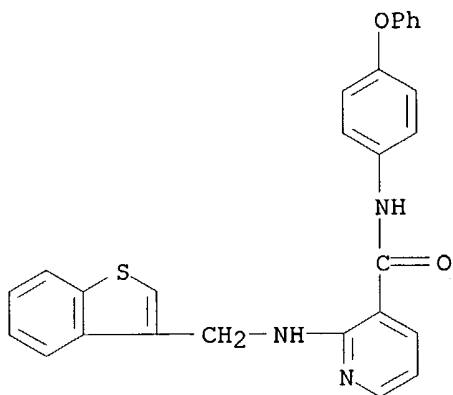
CN 3-Pyridinecarboxamide, N-[4-(pentafluoroethyl)-3-[(2R)-2-pyrrolidinylmethoxy]phenyl]-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 453562-48-6 CAPLUS

CN 3-Pyridinecarboxamide, 2-[(benzo[b]thien-3-ylmethyl)amino]-N-(4-phenoxyphenyl)- (9CI) (CA INDEX NAME)

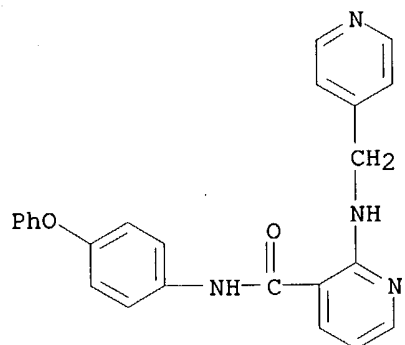


RN 453563-13-8 CAPLUS

CN 3-Pyridinecarboxamide, N-(4-phenoxyphenyl)-2-[(4-pyridinylmethyl)amino]-

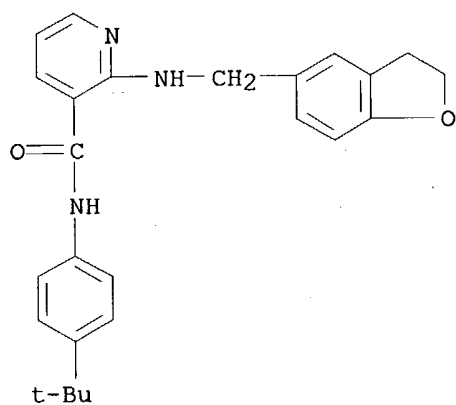
10/046,681

(9CI) (CA INDEX NAME)



RN 453563-27-4 CAPLUS

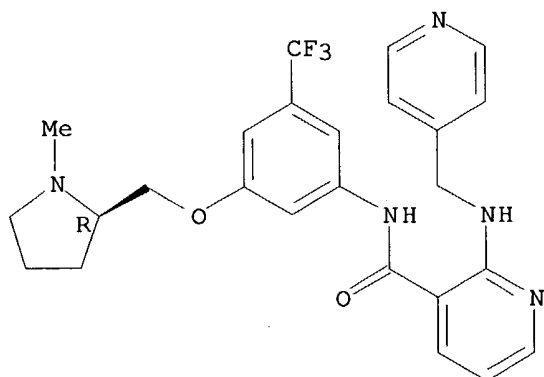
CN 3-Pyridinecarboxamide, 2-[[[(2,3-dihydro-5-benzofuranyl)methyl]amino]-N-[4-(1,1-dimethylethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 453563-62-7 CAPLUS

CN 3-Pyridinecarboxamide, N-[3-[[[(2R)-1-methyl-2-pyrrolidinyl]methoxy]-5-(trifluoromethyl)phenyl]-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

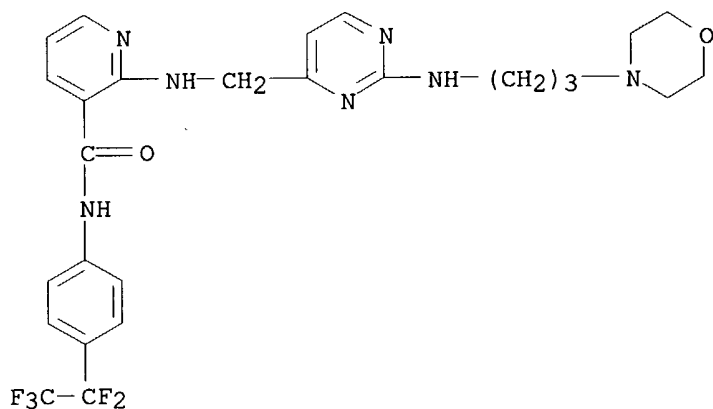
Absolute stereochemistry.



10/046,681

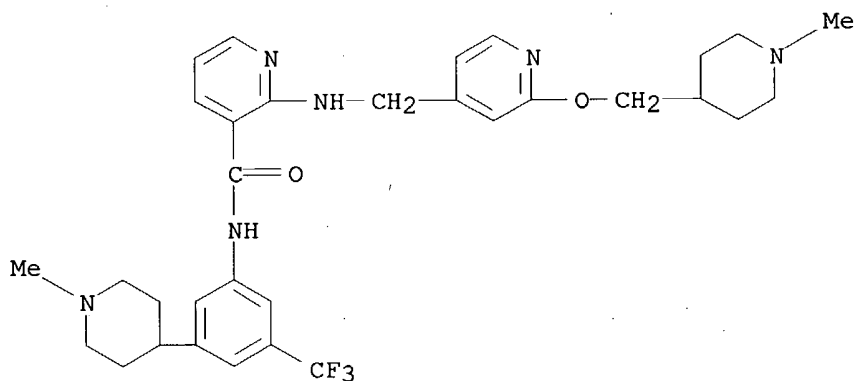
RN 453563-68-3 CAPLUS

CN 3-Pyridinecarboxamide, 2-[[[2-[[3-(4-morpholinyl)propyl]amino]-4-pyrimidinyl]methyl]amino]-N-[4-(pentafluoroethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 453563-72-9 CAPLUS

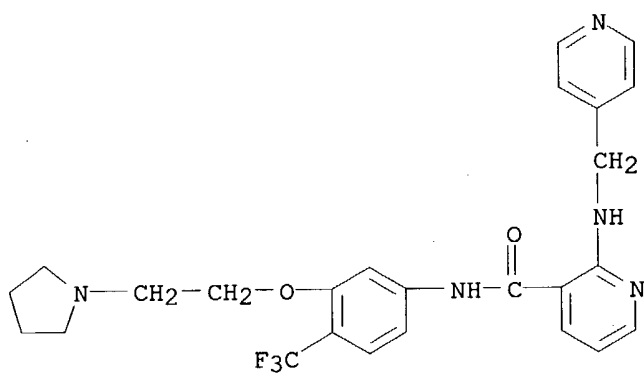
CN 3-Pyridinecarboxamide, 2-[[[2-[(1-methyl-4-piperidinyloxy)methyl]pyridin-4-yl]methyl]amino]-N-[3-(1-methyl-4-piperidinyloxy)-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



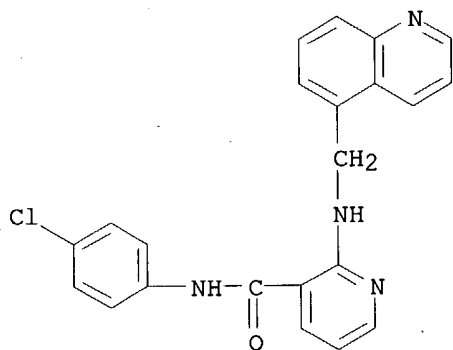
RN 453564-11-9 CAPLUS

CN 3-Pyridinecarboxamide, 2-[(4-pyridinylmethyl)amino]-N-[3-[2-(1-pyrrolidinyl)ethoxy]-4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

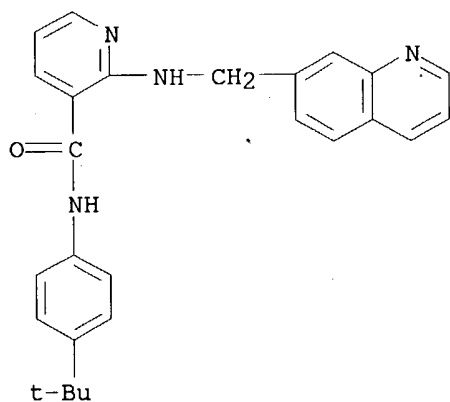
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RN 453564-46-0 CAPLUS
CN 3-Pyridinecarboxamide, N-(4-chlorophenyl)-2-[(5-quinolinylmethyl)amino]-
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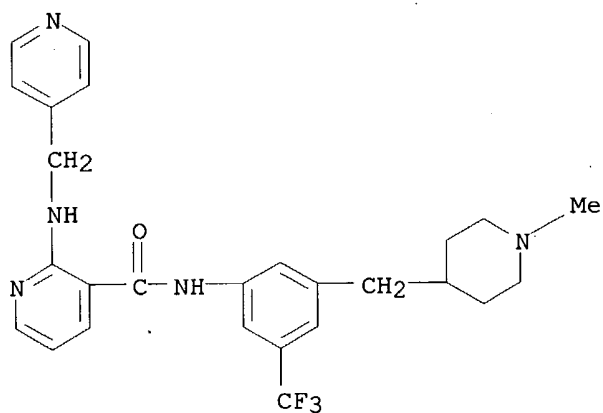


RN 453564-69-7 CAPLUS
CN 3-Pyridinecarboxamide, N-[4-(1,1-dimethylethyl)phenyl]-2-[(7-quinolinylmethyl)amino]- (9CI) (CA INDEX NAME)



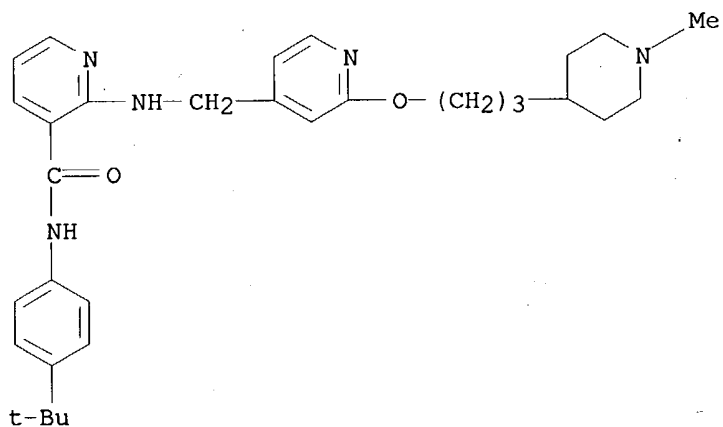
RN 453564-89-1 CAPLUS
CN 3-Pyridinecarboxamide, N-[3-[(1-methyl-4-piperidinyl)methyl]-5-(trifluoromethyl)phenyl]-2-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

10/046,681



RN 453564-94-8 CAPLUS

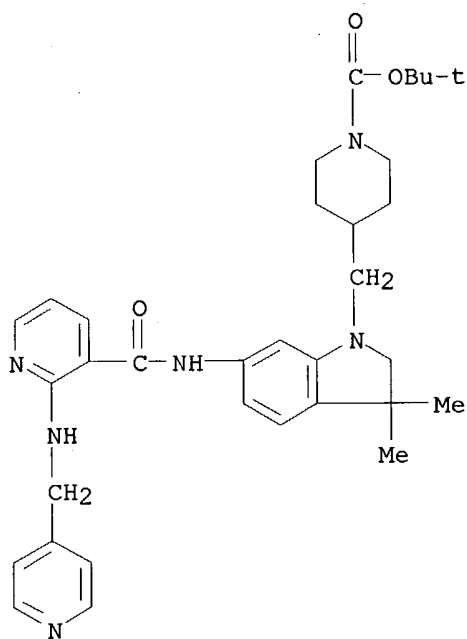
CN 3-Pyridinecarboxamide, N-[4-(1,1-dimethylethyl)phenyl]-2-[[[2-[3-(1-methyl-4-piperidinyl)propoxy]-4-pyridinyl]methyl]amino]- (9CI) (CA INDEX NAME)



RN 453564-98-2 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[[2,3-dihydro-3,3-dimethyl-6-[[[2-[(4-pyridinylmethyl)amino]-3-pyridinyl]carbonyl]amino]-1H-indol-1-yl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

10/046,681



REFERENCE COUNT:

19

THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT